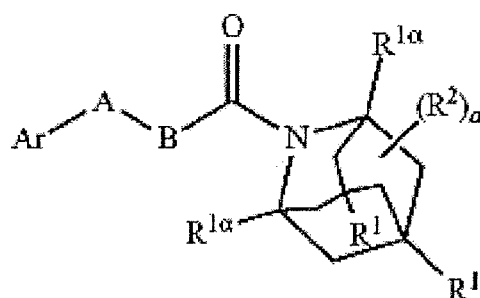


Claims

1. A compound of formula (I):

Formula (I)



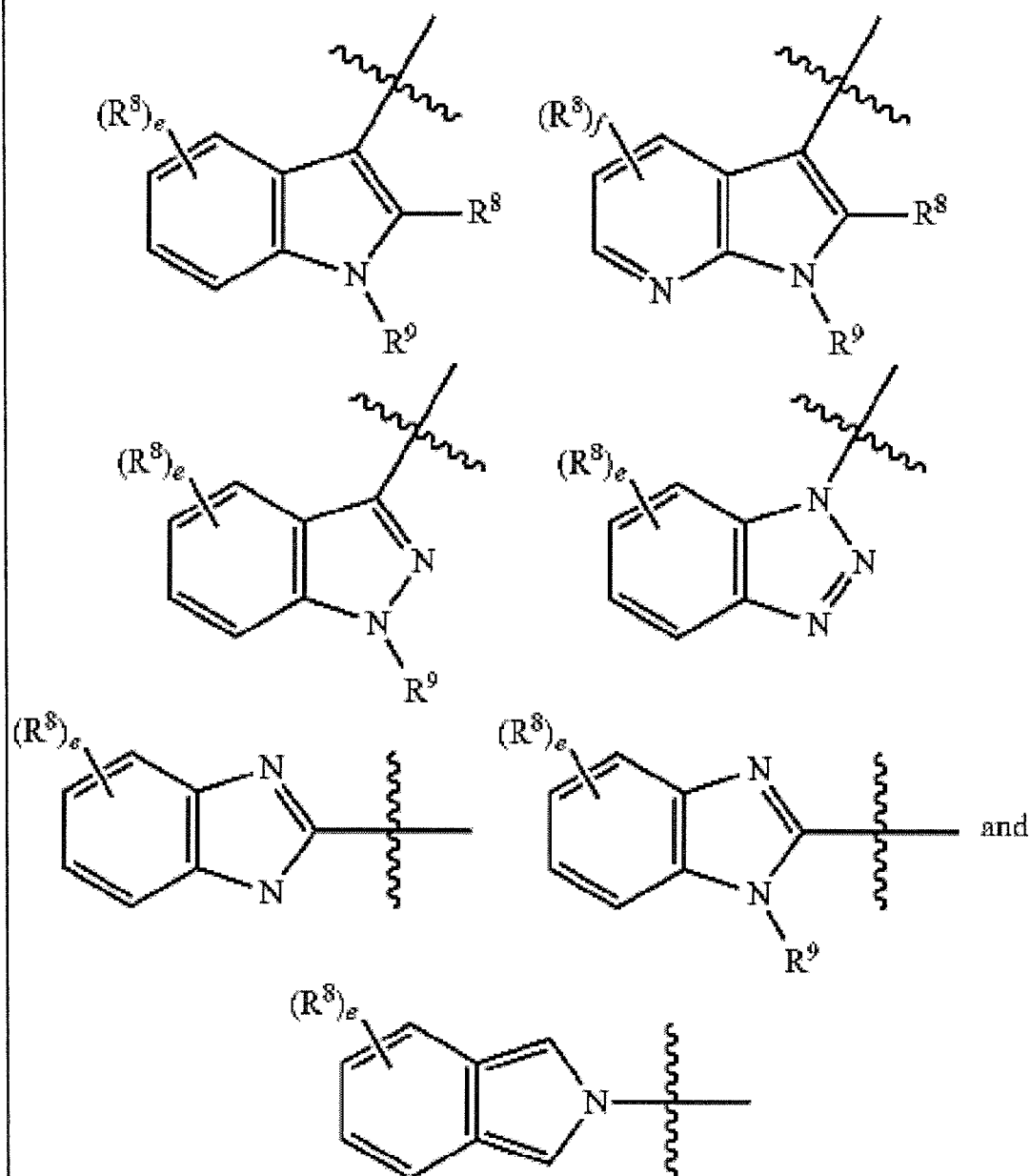
wherein:

each R^1 is independently selected from the group consisting of H, OH, OCF_2H , OCH_3 , CH_3 , F, Br, Cl, CN, O-cyclopropyl, CO_2H , $CONH_2$, $CONHPh$, $CONH(4-flouroPh)$, CH_2OH , tetrazole, CH_2CO_2H , $CH_2CH_2CO_2H$, CCH_3HCO_2H , CH_2NH_2 , NH_2 and $NHCH_3$,

$R^{1\alpha}$ is H;

R^2 is selected from the group consisting of H, OH, CO_2H and tetrazole;

Ar is selected from the group consisting of:



e is an integer selected from the group consisting of 0, 1, 2, 3, and 4;

f is an integer selected the group consisting of 0, 1, 2, and 3;

wherein each R^8 is independently selected from the group consisting of H, halogen, OH, NO_2 , CN, SH, NH_2 , CF_3 , OCF_3 , optionally substituted C_1 - C_{12} alkyl, optionally substituted C_1 - C_{12} haloalkyl, optionally substituted C_2 - C_{12} alkenyl, optionally substituted C_2 - C_{12} alkynyl, optionally substituted C_2 - C_{12} heteroalkyl, optionally substituted C_3 - C_{12} cycloalkyl, optionally substituted C_3 - C_{12} cycloalkenyl, optionally substituted C_2 - C_{12} heterocycloalkyl, optionally substituted C_2 - C_{12} heterocycloalkenyl, optionally substituted C_6 - C_{18} aryl, optionally substituted C_1 - C_{18} heteroaryl, optionally substituted C_1 - C_{12} alkyloxy, optionally substituted C_2 - C_{12} alkenyloxy, optionally substituted C_2 - C_{12} alkynyloxy, optionally substituted C_2 - C_{10} heteroalkyloxy, optionally substituted C_3 - C_{12} cycloalkyloxy, optionally substituted C_3 - C_{12} cycloalkenyloxy, optionally substituted C_2 - C_{12} heterocycloalkyloxy, optionally substituted C_2 - C_{12} heterocycloalkenyloxy, optionally substituted C_6 - C_{18} aryloxy, optionally substituted C_1 - C_1 heteroaryloxy, optionally substituted C_1 - C_{12} alkylamino, SR^{10} , SO_3H , $SO_2NR^{10}R^{11}$, SO_2R^{10} , OSO_2R^{10} , $SONR^{10}R^{11}$, SOR^{10} , COR^{10} , $COOH$, $COOR^{10}$, $CONR^{10}R^{11}$, $NR^{10}COR^{11}$, $NR^{10}COOR^{11}$, $NR^{10}SO_2R^{11}$, $NR^{10}CONR^{10}R^{11}$, and $NR^{10}R^{11}$;

wherein R^9 is selected from the group consisting of H, optionally substituted C_1 - C_{12} alkyl, optionally substituted C_2 - C_{12} alkenyl, optionally substituted C_2 - C_{12} alkynyl, optionally substituted C_2 - C_{12} heteroalkyl, optionally substituted C_3 - C_{12} cycloalkyl, optionally substituted C_2 - C_{12} heterocycloalkyl, optionally substituted C_6 - C_{18} aryl, optionally substituted C_1 - C_{18} heteroaryl,

SO_3H , $\text{SO}_2\text{NR}^{10}\text{R}^{11}$, SO_2R^{10} , $\text{SONR}^{10}\text{R}^{11}$, SOR^{10} , COR^{10} , COOH , COOR^{10} , and $\text{CONR}^{10}\text{R}^{11}$;

wherein each R^{10} and R^{11} is independently selected from the group consisting of H, optionally substituted $\text{C}_1\text{-C}_{12}$ alkyl, optionally substituted $\text{C}_2\text{-C}_{10}$ heteroalkyl, optionally substituted $\text{C}_1\text{-C}_{12}$ haloalkyl, optionally substituted $\text{C}_3\text{-C}_{12}$ cycloalkyl, optionally substituted $\text{C}_6\text{-C}_{18}$ aryl, and optionally substituted $\text{C}_1\text{-C}_{18}$ heteroaryl;

A is $\text{—CR}^a\text{R}^b\text{—}$;

B is a group of the formula $\text{—(CR}^c\text{R}^d)_n\text{—}$;

wherein each R^a , and R^b , is independently selected from the group consisting of H, halogen, OH, NO_2 , CN, SH, NH_2 , CF_3 , OCF_3 , methyl, ethyl, propyl, isopropyl, cyclopropyl, phenyl, 4-chloro-phenyl, 4-fluoro-phenyl, thiophene-2-yl,

or any two R^a , and R^b , on the same carbon atom when taken together form a cyclopropyl group;

R^c and R^d are both H;

n is an integer selected from the group consisting of 0 and 1;

a is an integer selected from the group consisting of 0, and 1,

or a pharmaceutically acceptable salt thereof.

2. A compound according to claim 1 wherein B is CH_2 .

3. A compound according to claim 1 wherein R^a and R^b are different.

4. A compound according to claim 3 wherein one of R^a and R^b is H and the other is selected from the group consisting of methyl, ethyl, propyl, and isopropyl.

5. A compound according to claim 1 wherein the R^8 substituent is located in the 4 or the 5 position of the six membered ring.

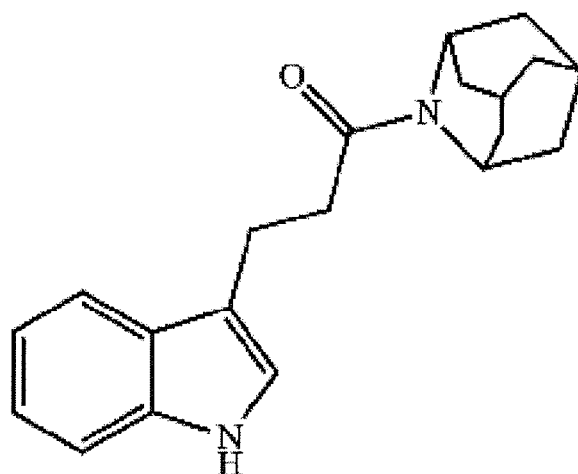
6. A compound according to claim 1 wherein each R^8 is independently selected from the group consisting of CH_3 , CH_2CH_3 , $CH_2CH_2CH_3$, $CH(CH_3)_2$, $(CH_2)_3CH_3$, Cl, Br, F, I, OH, NO_2 , NH_2 , CN, SO_3H , OCH_3 , $OCH_2CH_2CH_3$, CF_3 , and OCF_3 .

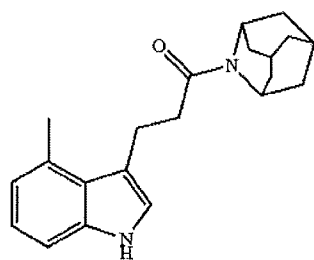
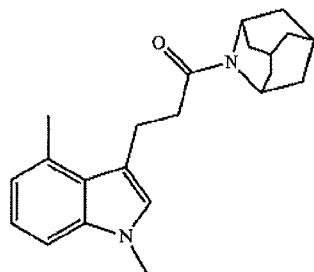
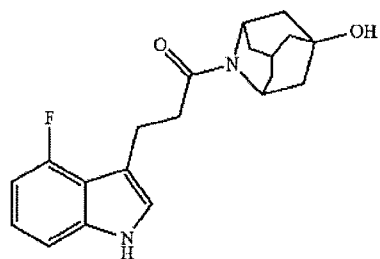
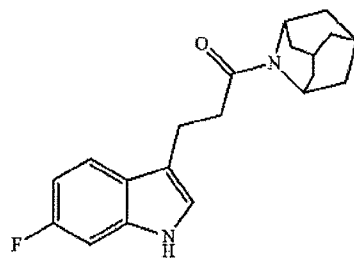
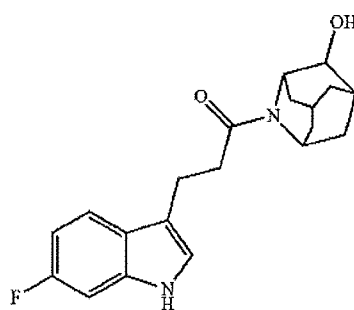
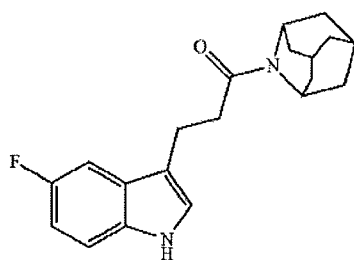
7. A compound according to claim 1 wherein a is 0.

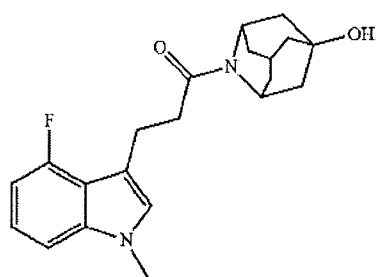
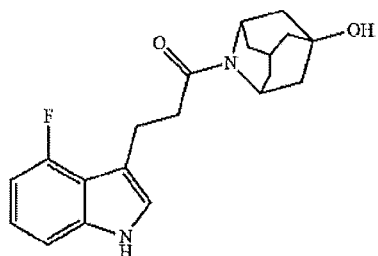
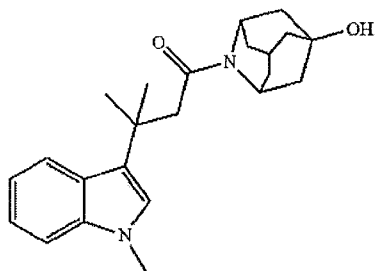
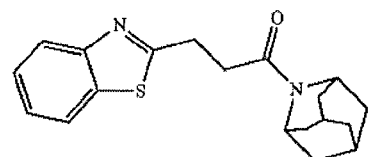
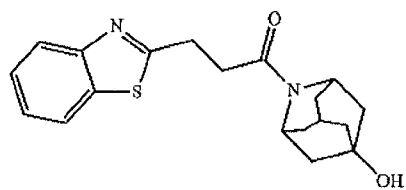
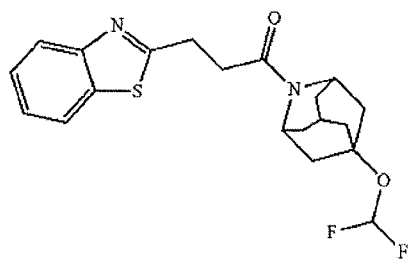
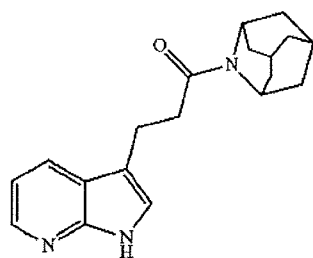
8. A compound according to claim 1 wherein each R^1 is independently selected from the group consisting of H, OH, F, Cl, Br, CO_2H , $CONH_2$, CH_2OH , CN, OCH_3 , and $OCHF_2$.

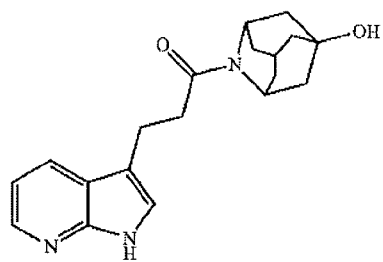
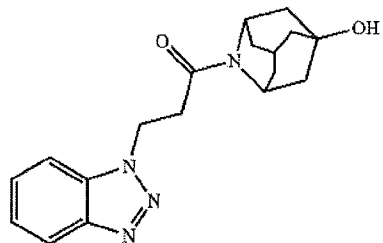
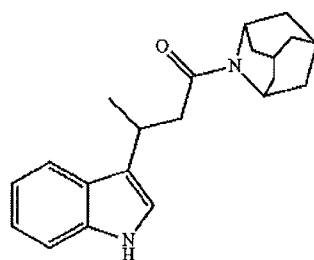
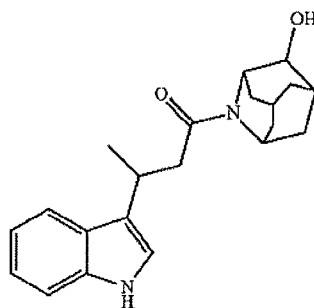
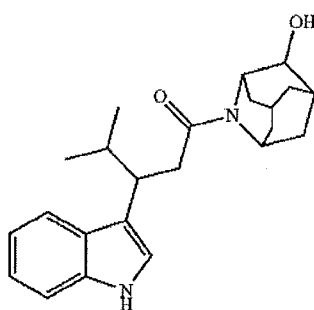
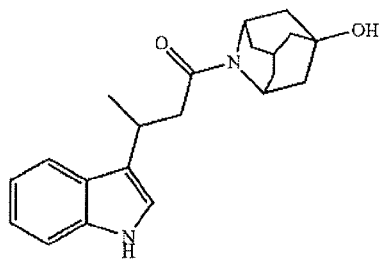
9. A compound according to claim 1 wherein one R^1 is H and the other R^1 is OH.

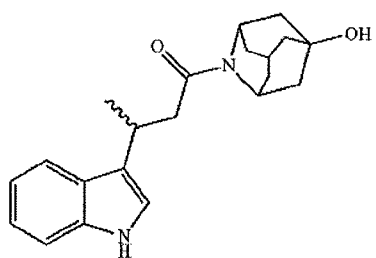
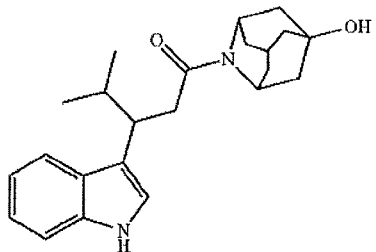
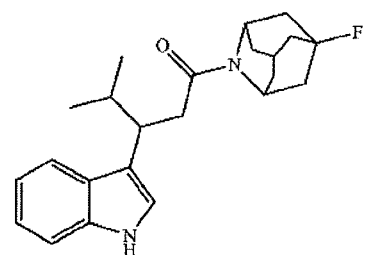
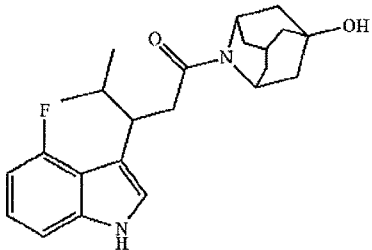
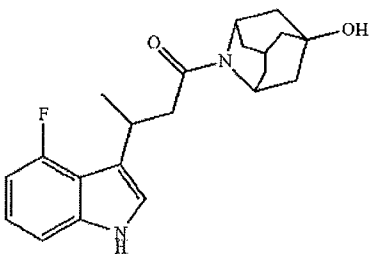
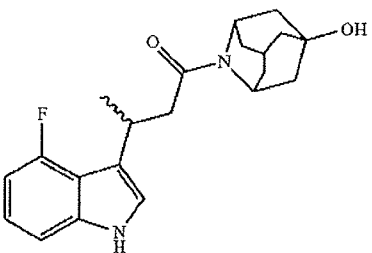
10. A compound according to claim 1 selected from the group consisting of:

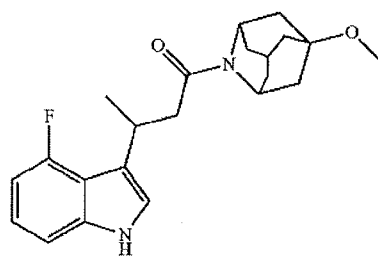
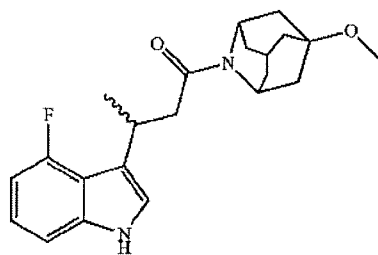
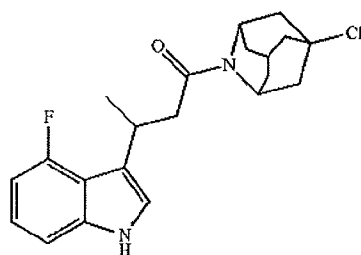
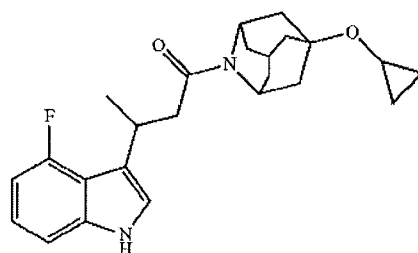
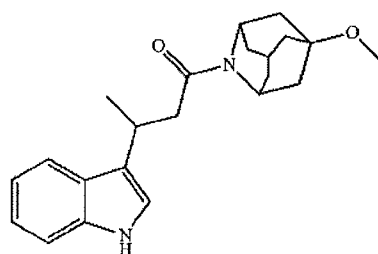
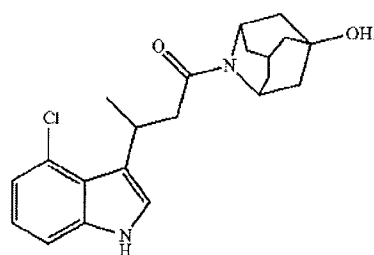


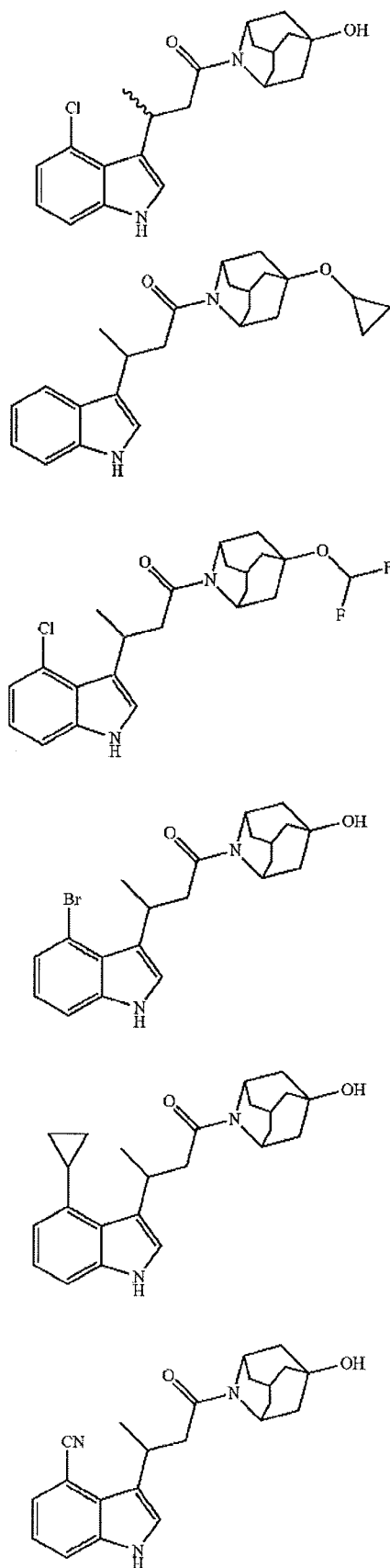


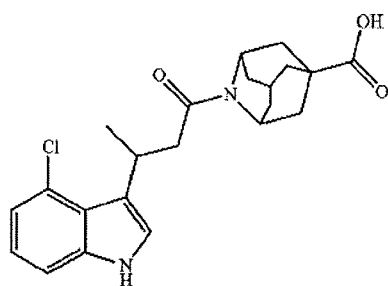
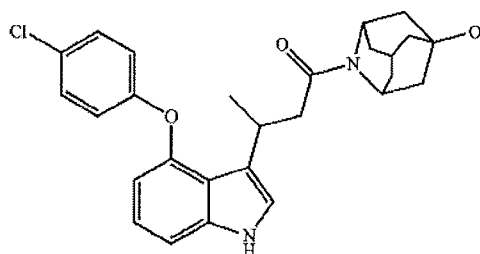
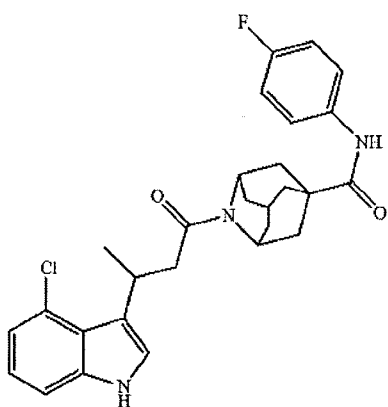
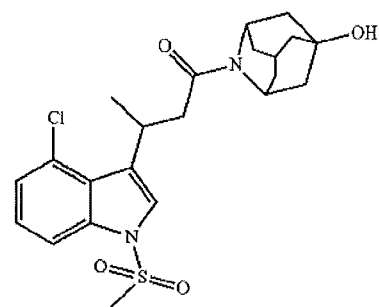
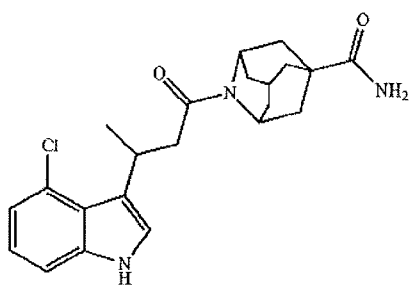


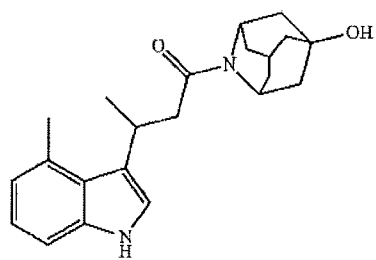
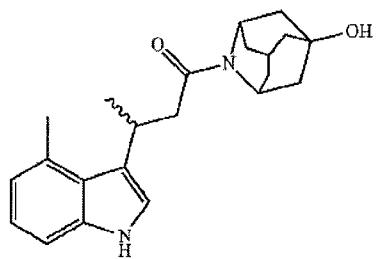
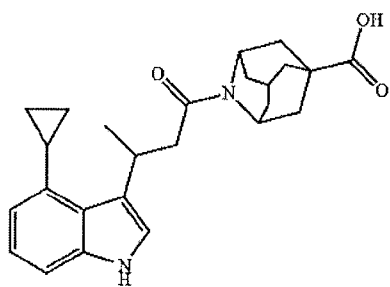
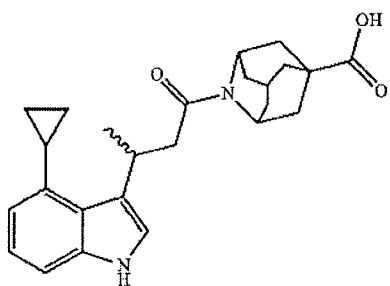
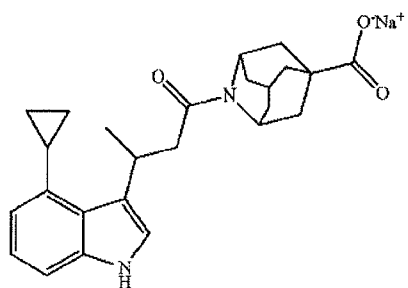
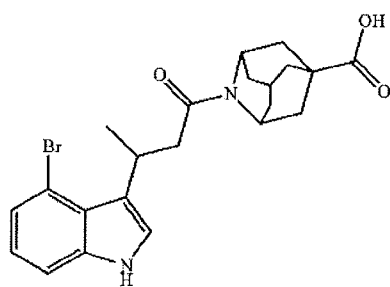


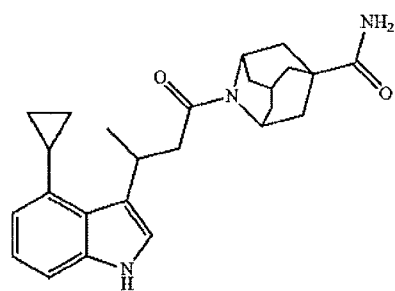
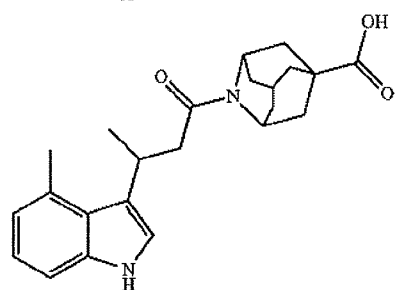
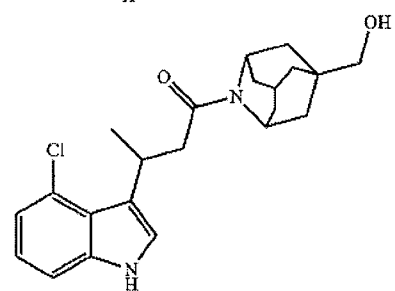
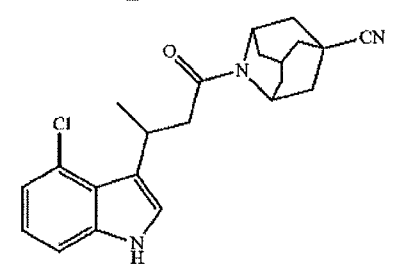
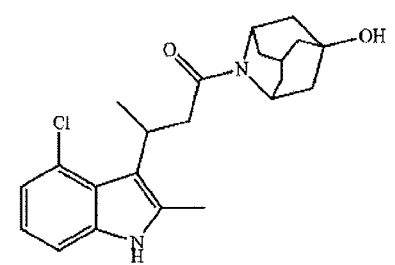
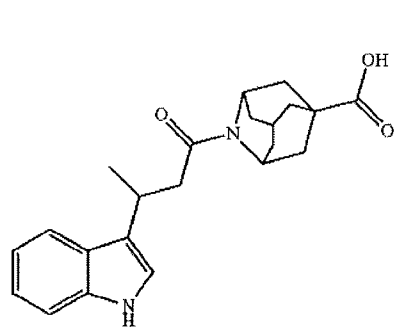


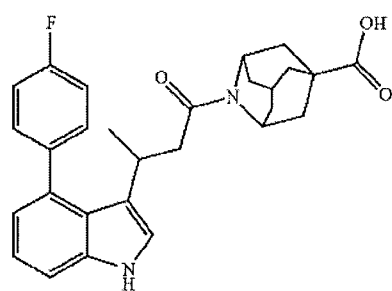
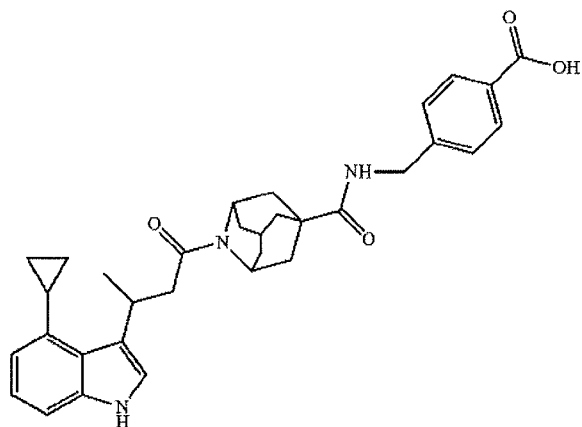
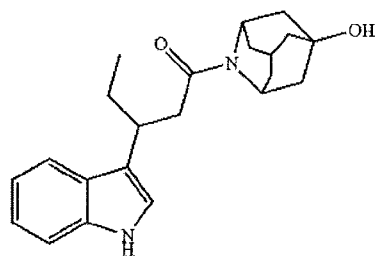
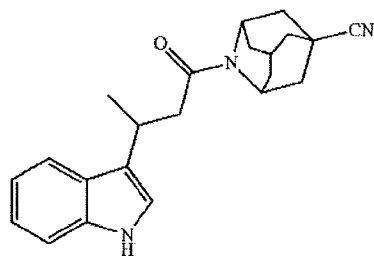
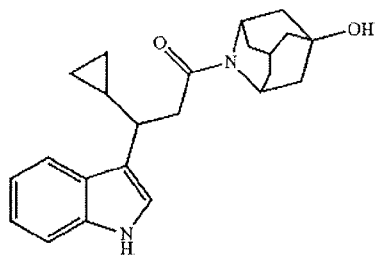


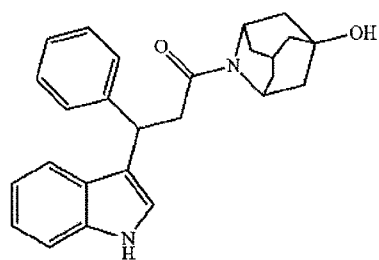
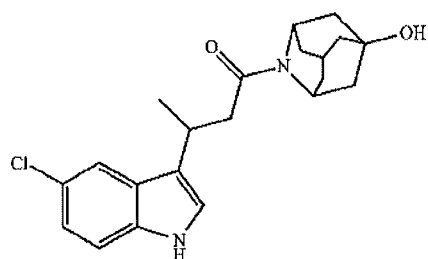
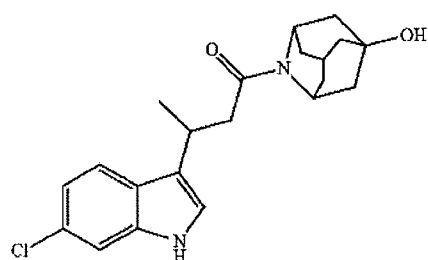
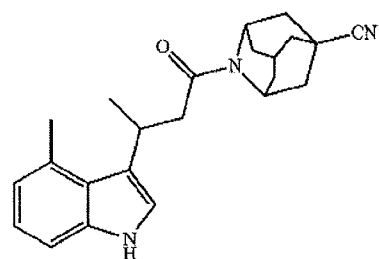
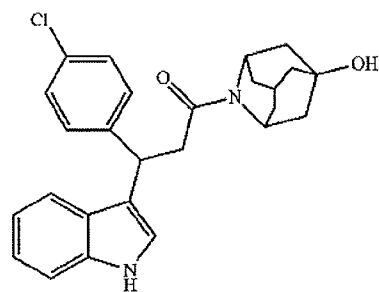
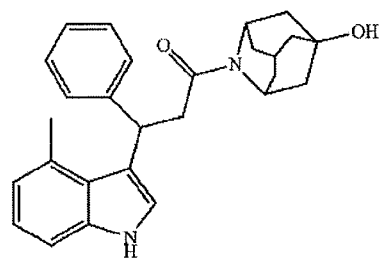


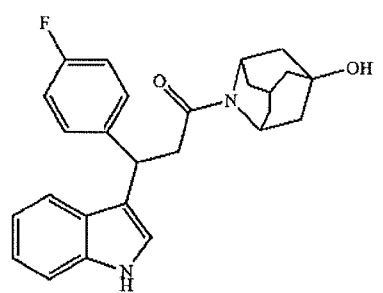
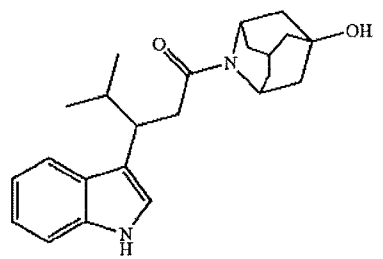
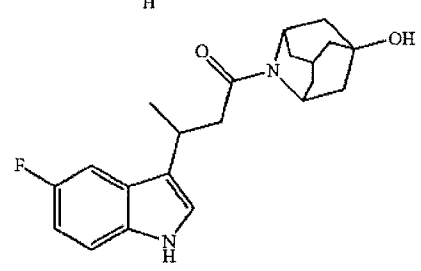
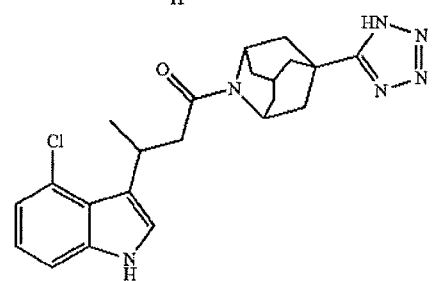
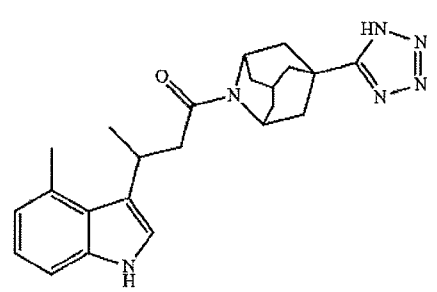
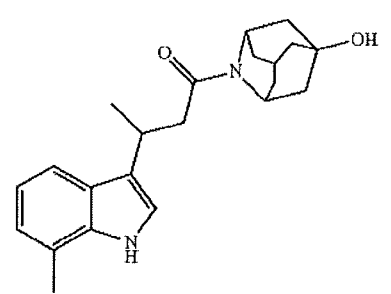


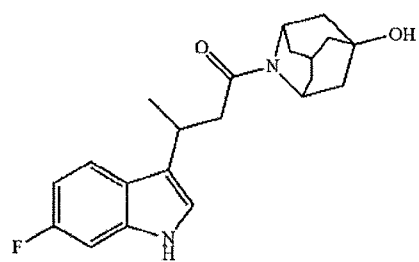
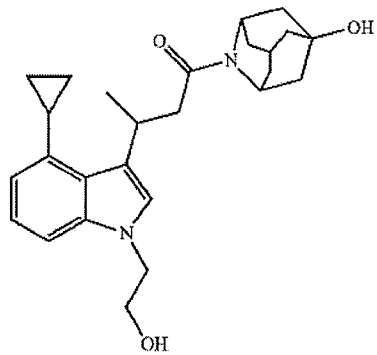
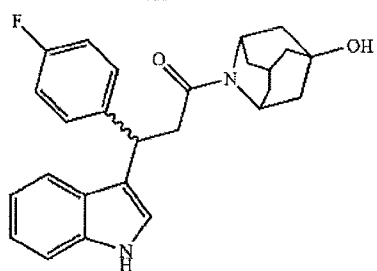
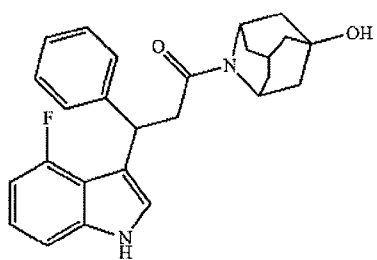
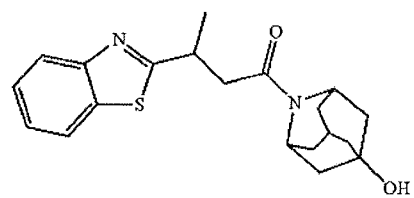
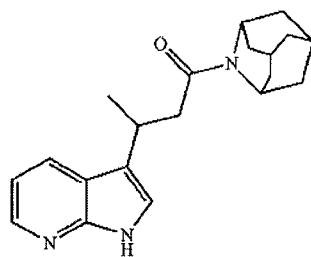


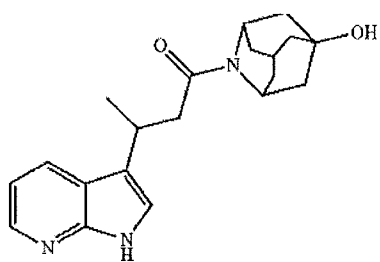
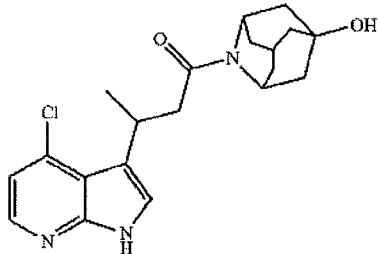
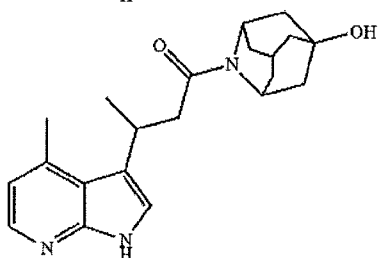
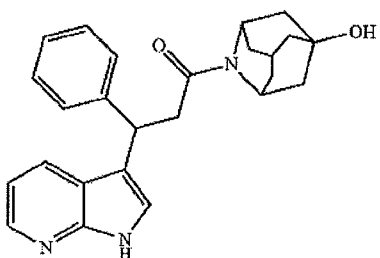
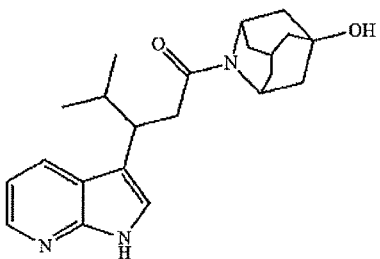
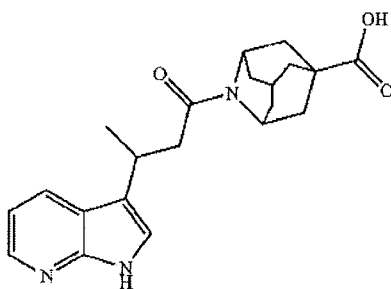


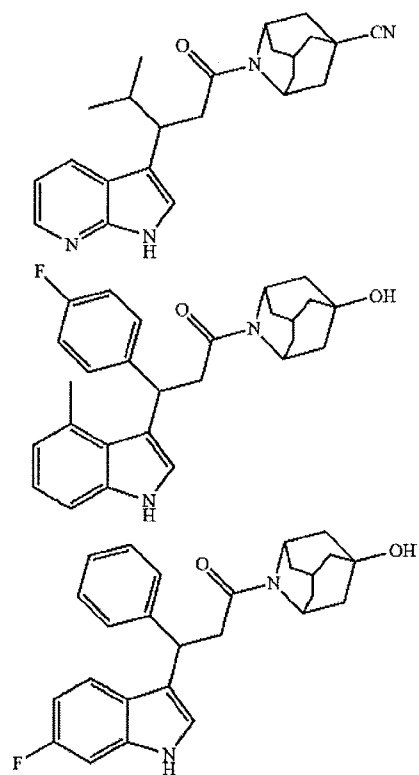
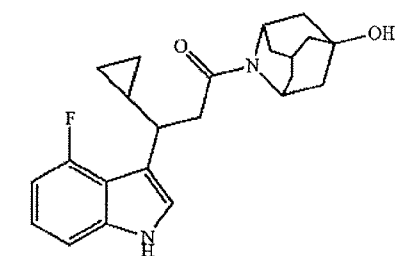
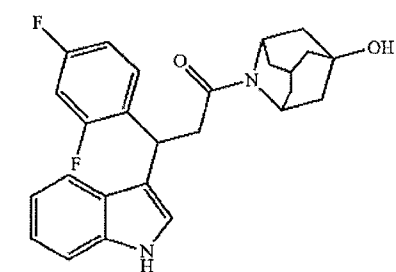
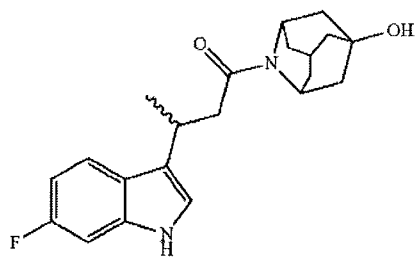


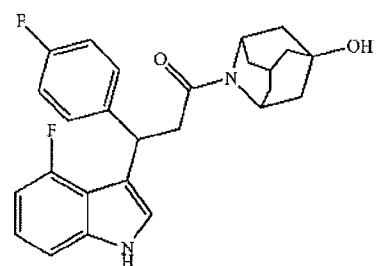
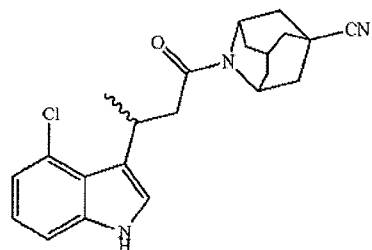
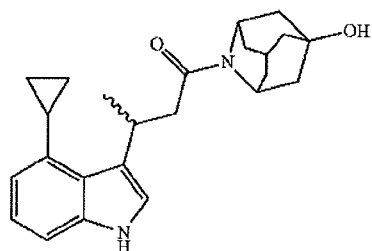
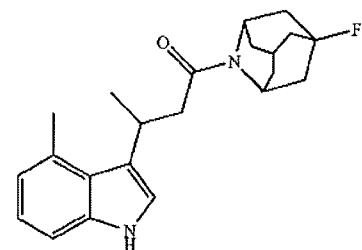
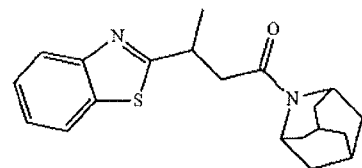
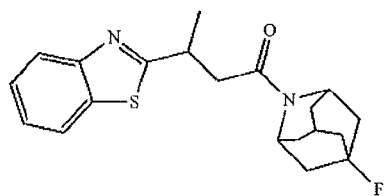
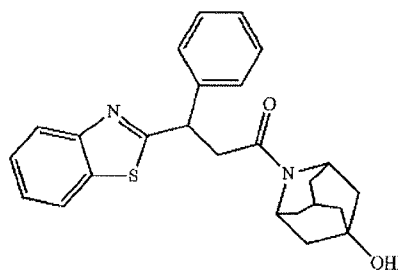


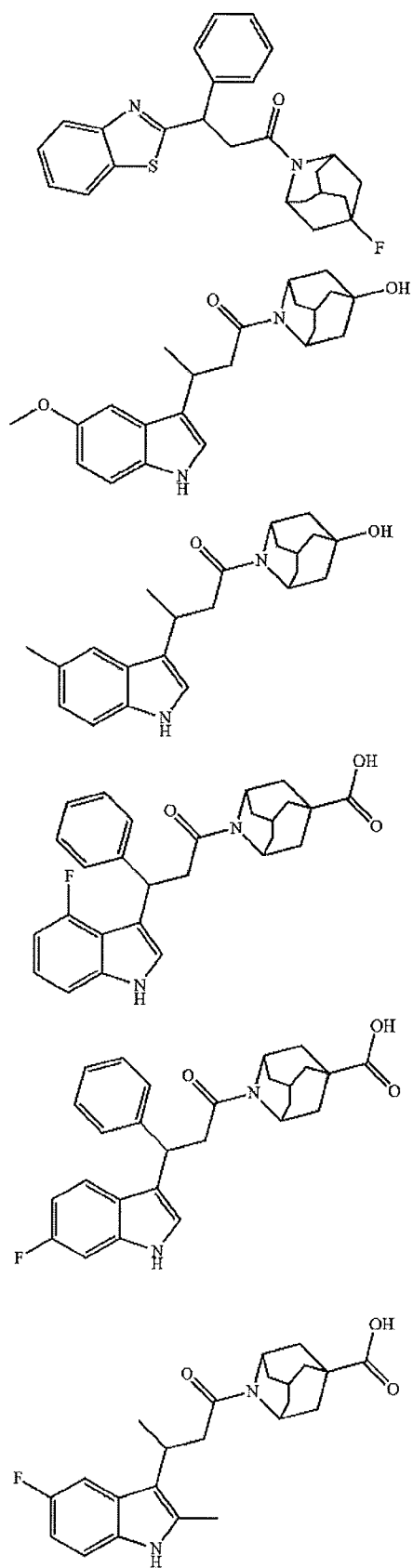


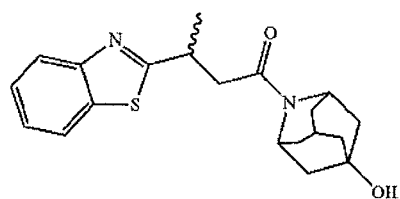
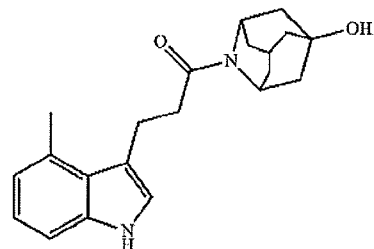
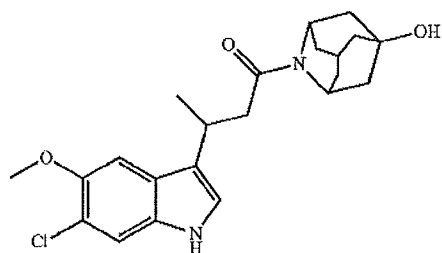
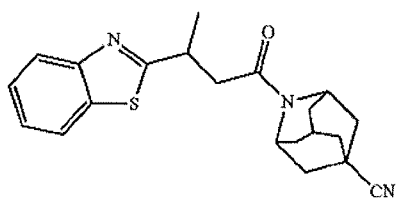
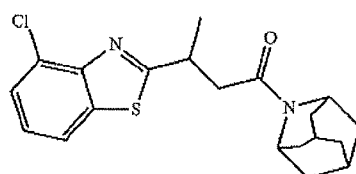
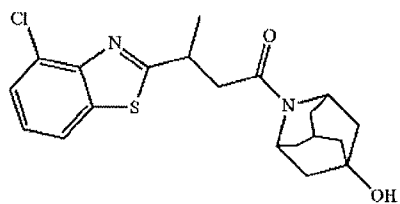
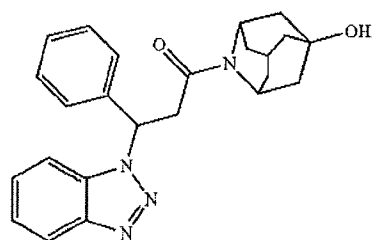


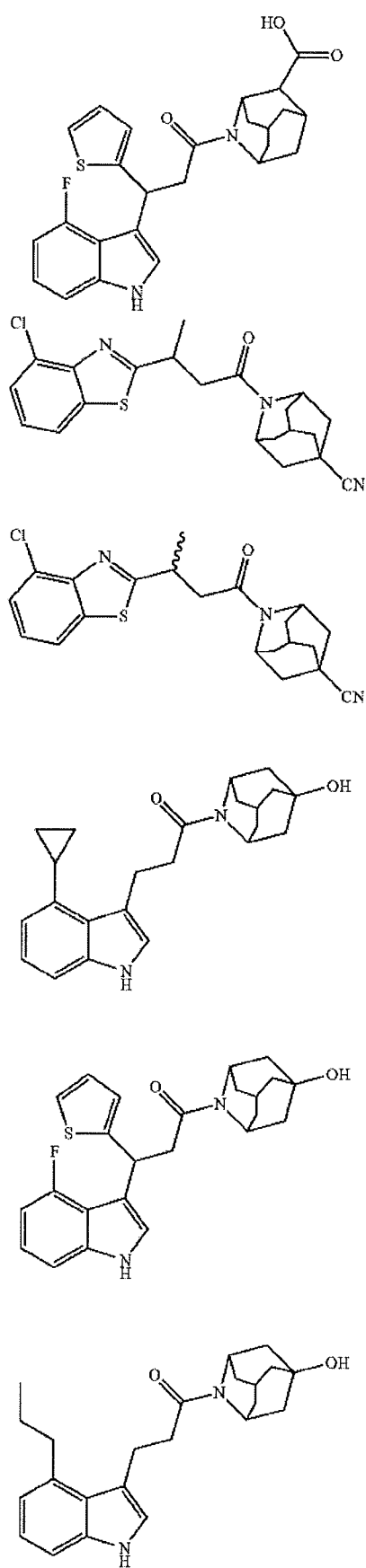


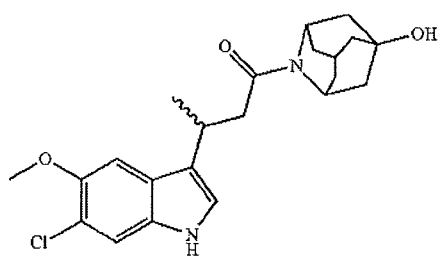
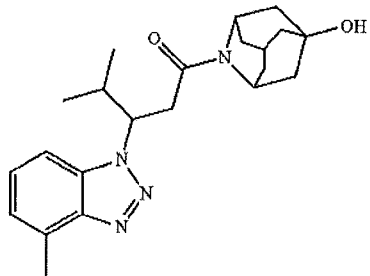
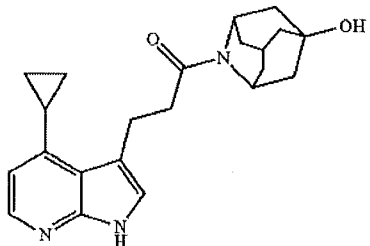
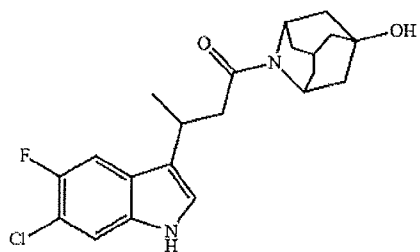
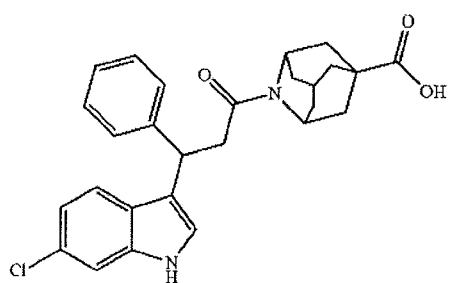
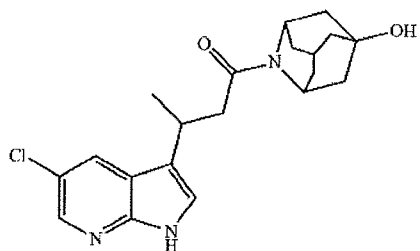


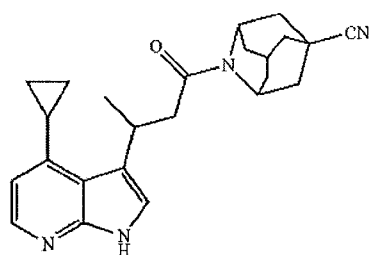
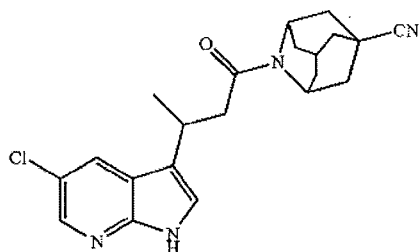
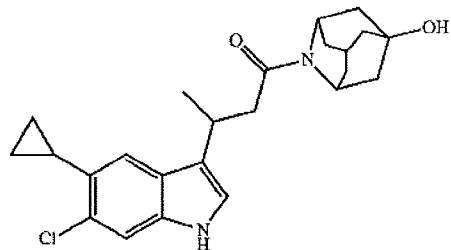
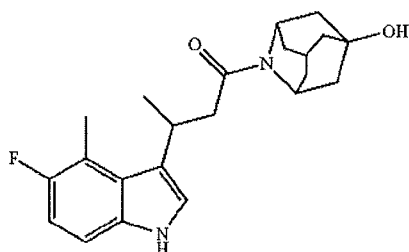
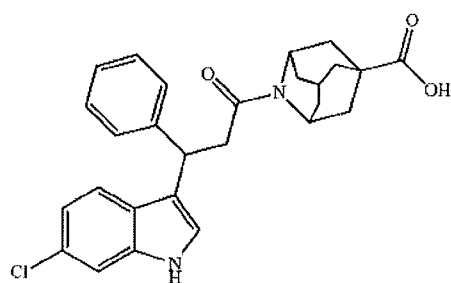
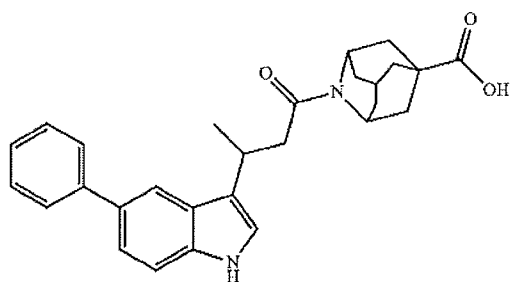


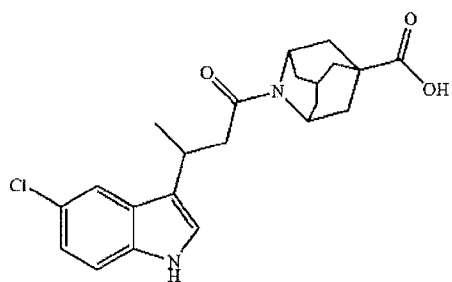
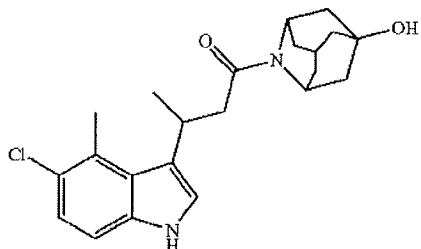
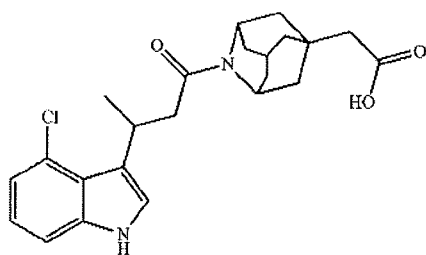
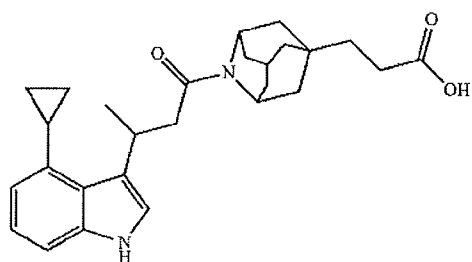
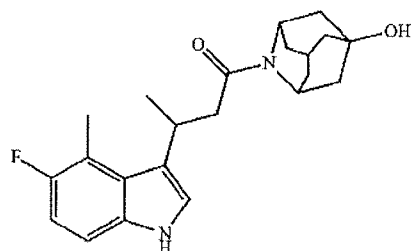
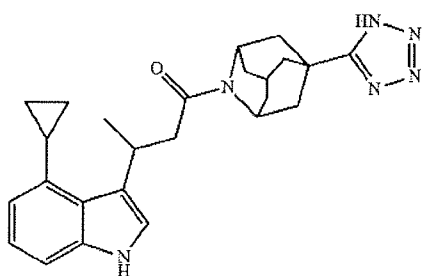


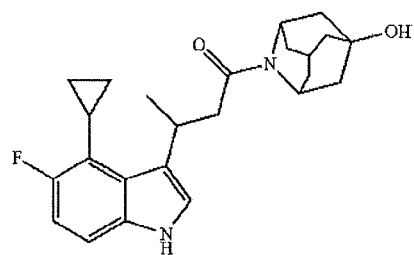
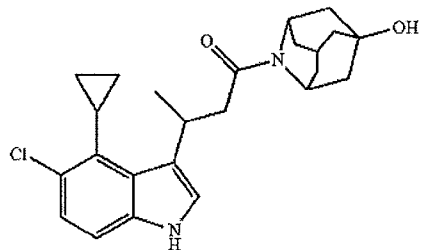
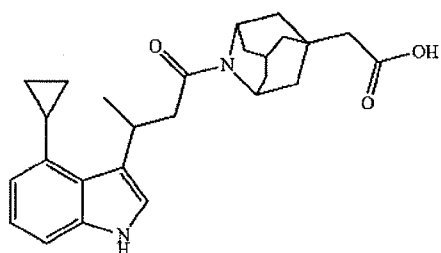
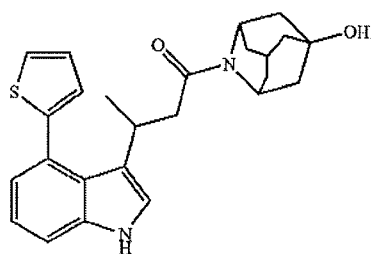
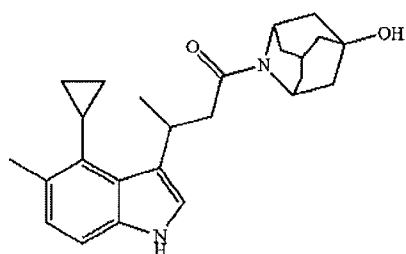
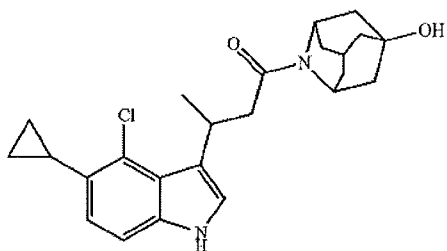


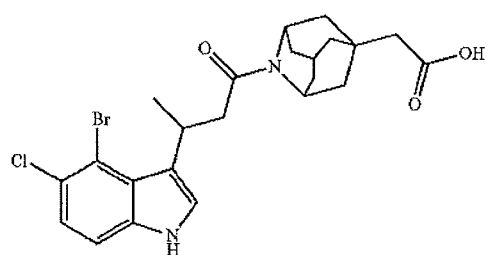
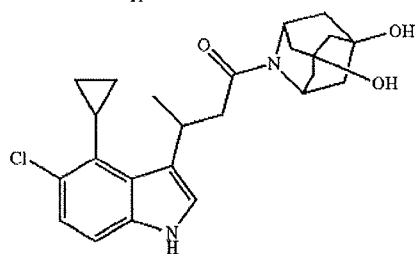
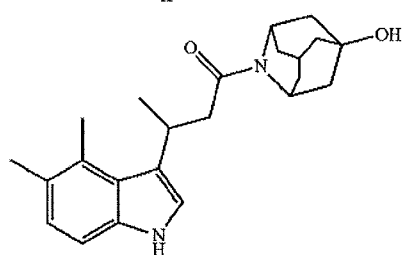
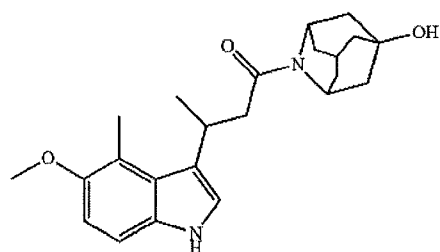
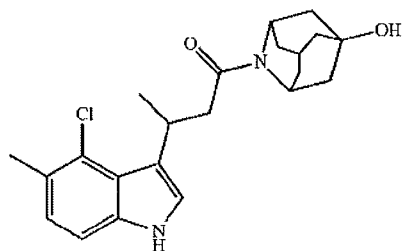
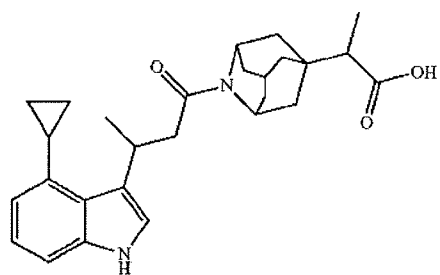


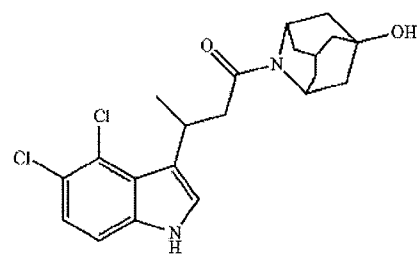
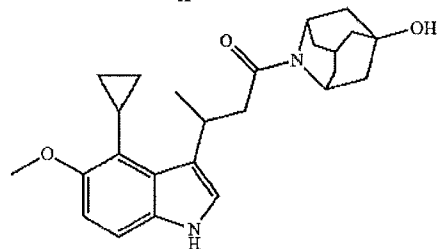
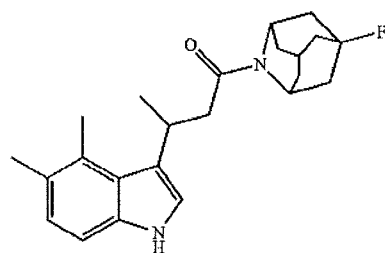
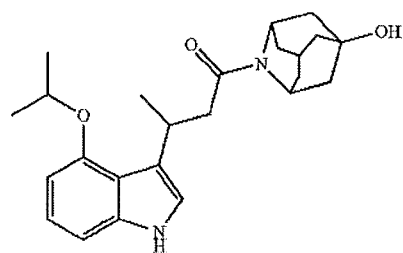
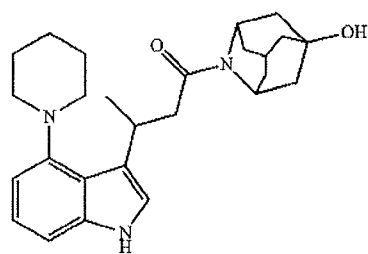
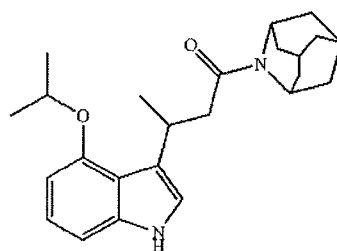


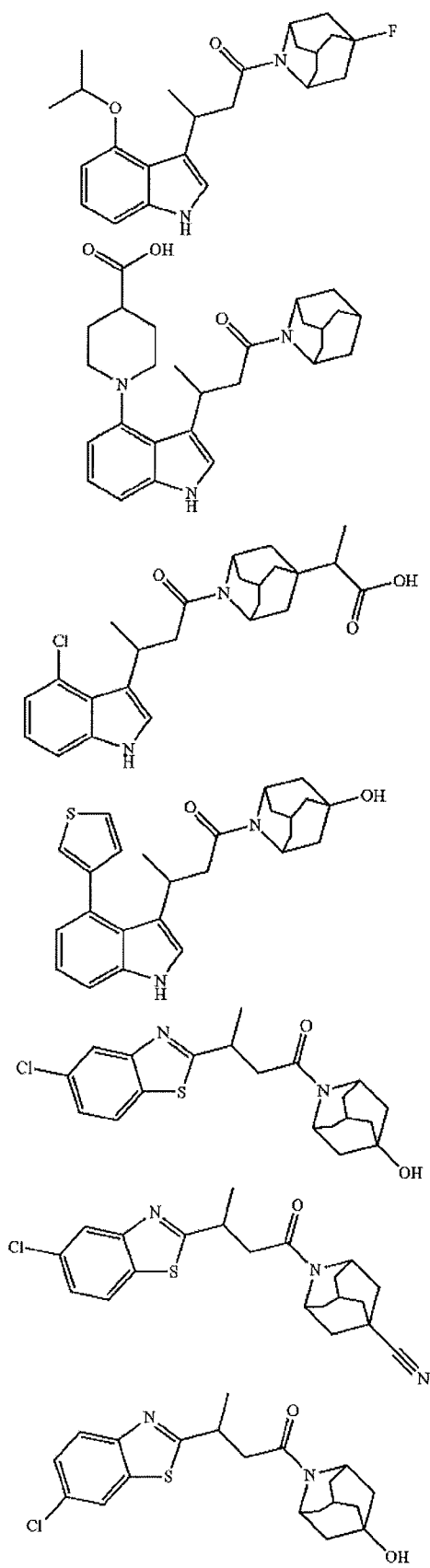


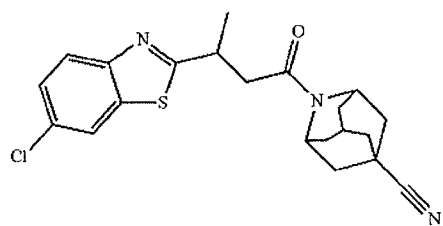
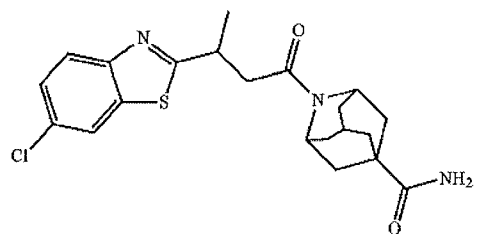
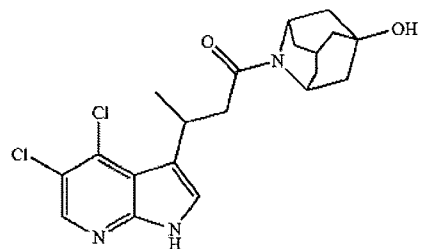
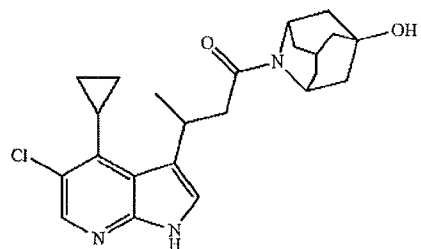
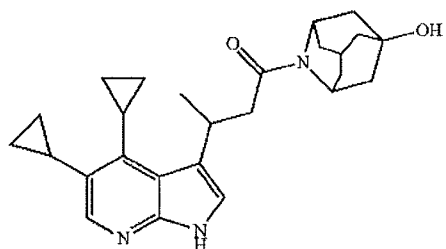
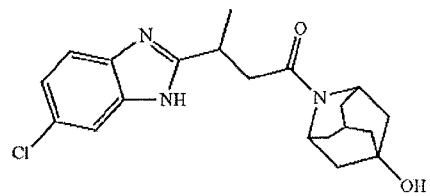
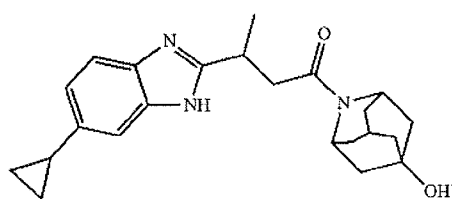


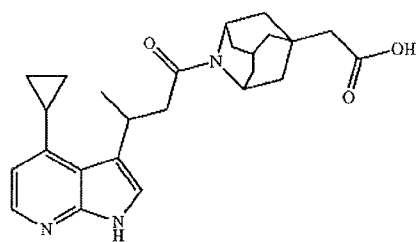
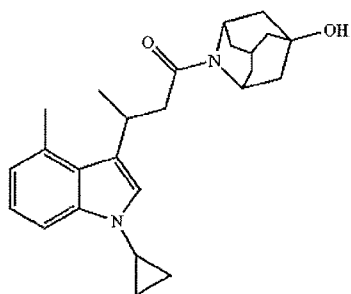
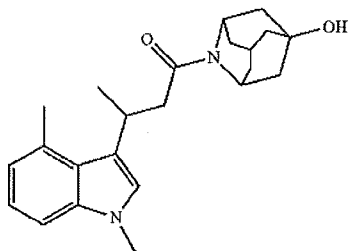
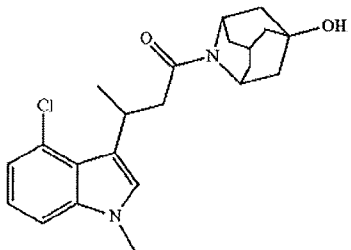
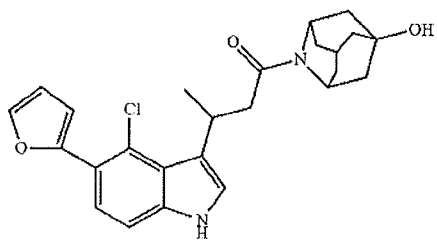
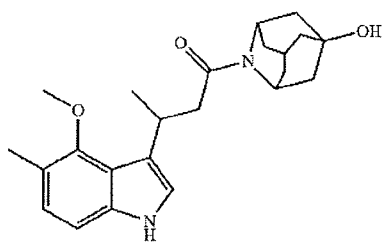


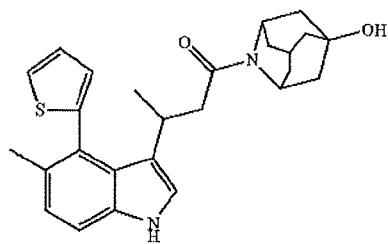
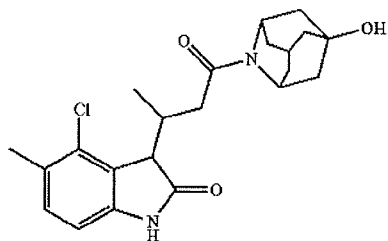
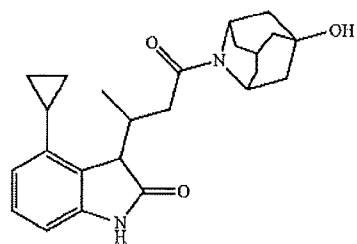
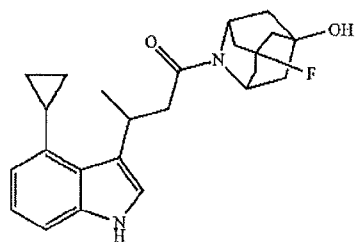
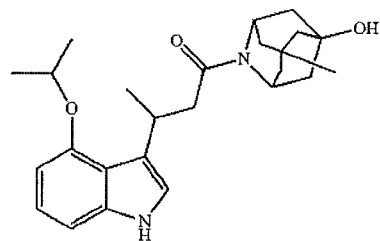
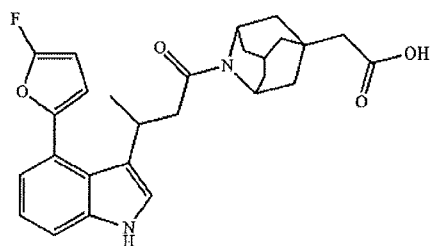


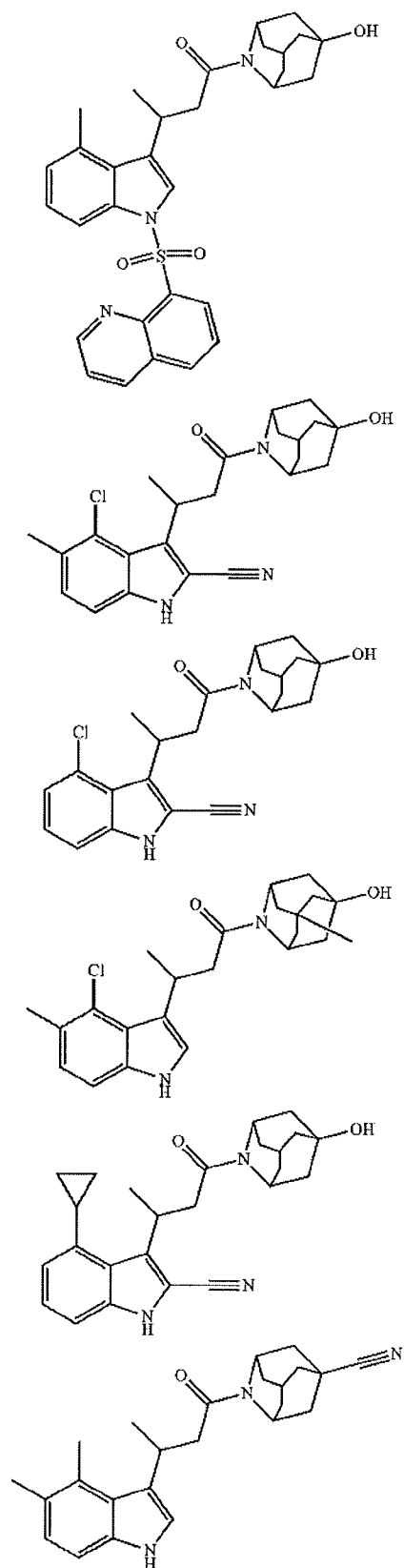


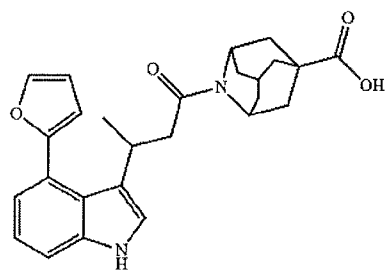
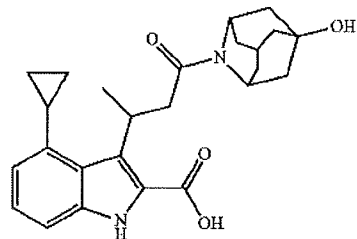
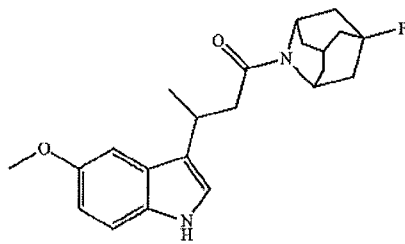
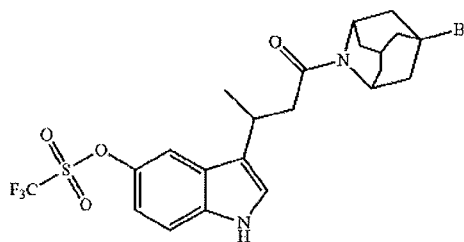
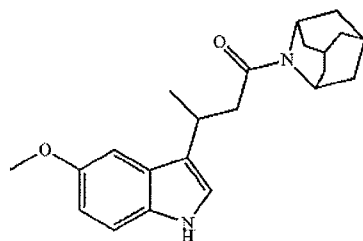
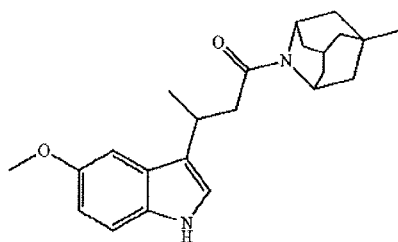


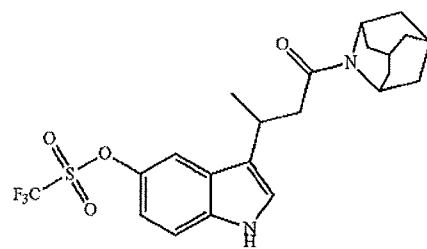
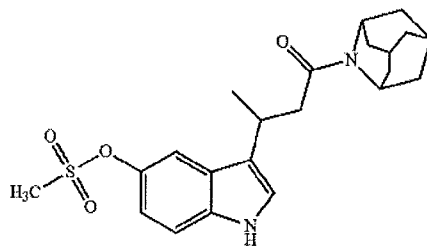
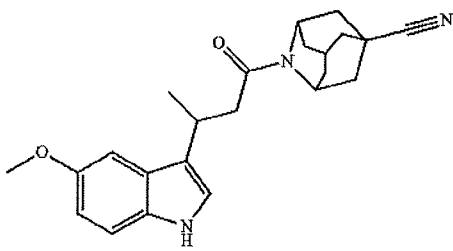
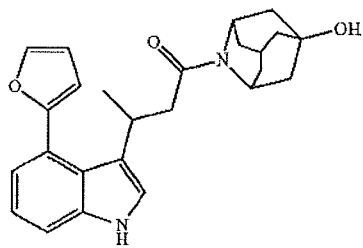
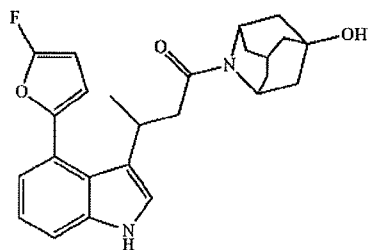
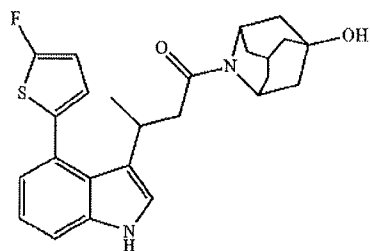


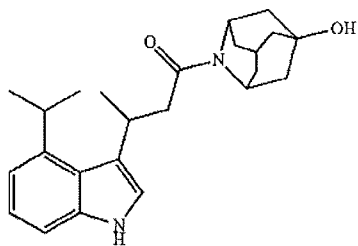
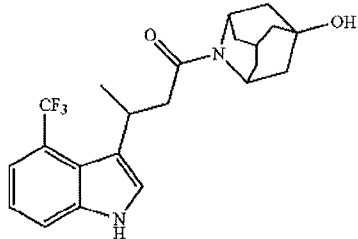
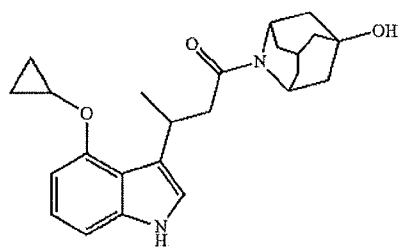
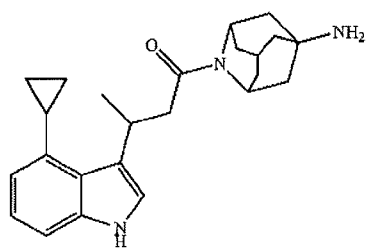
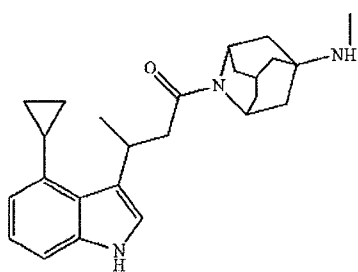
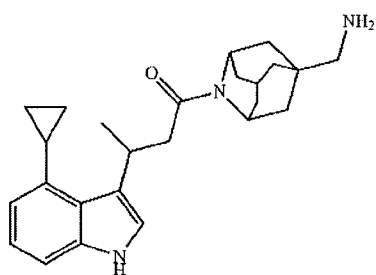


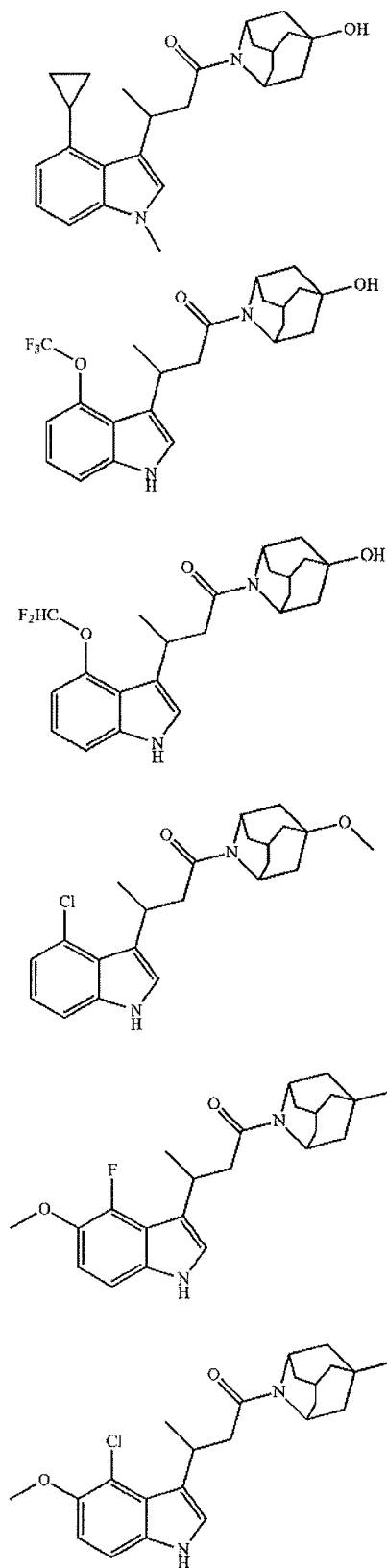


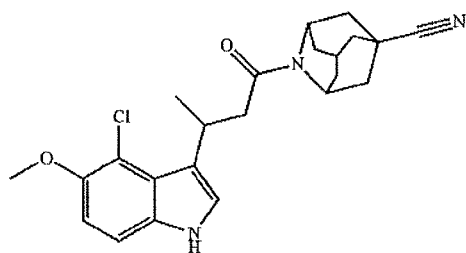
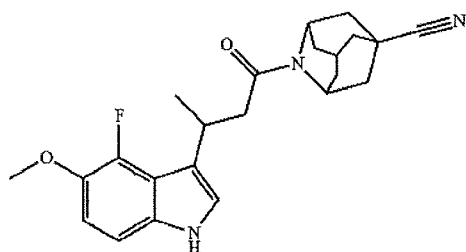
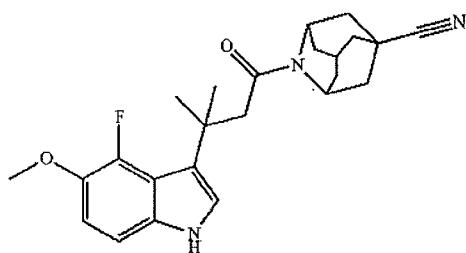
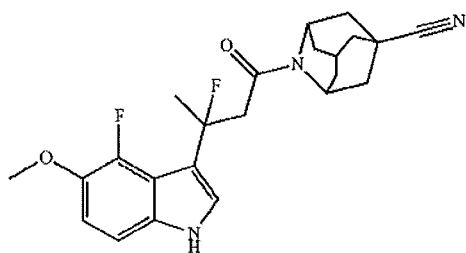
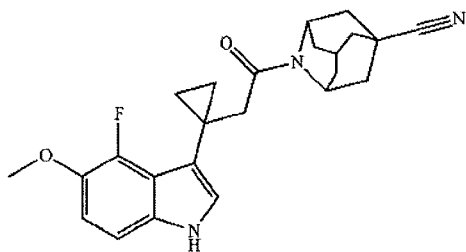
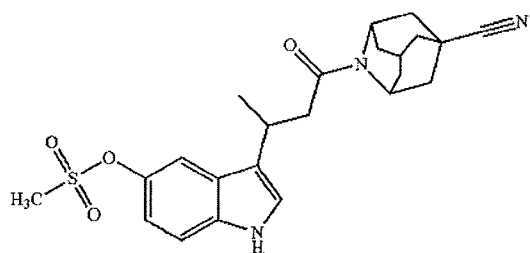


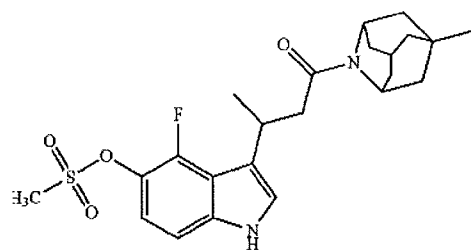
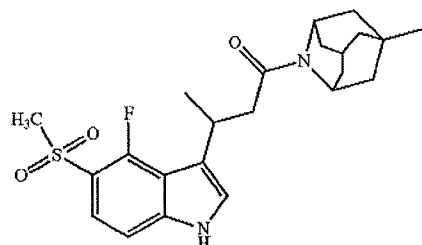
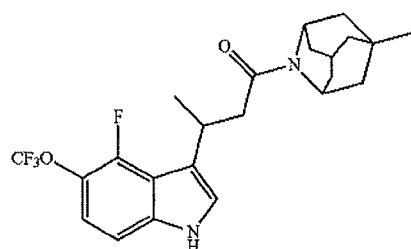
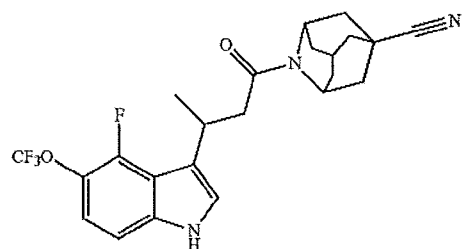
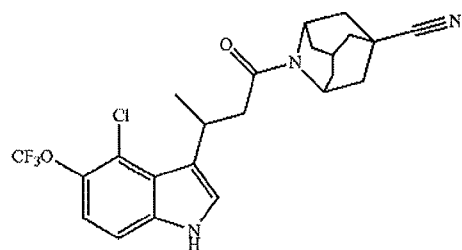
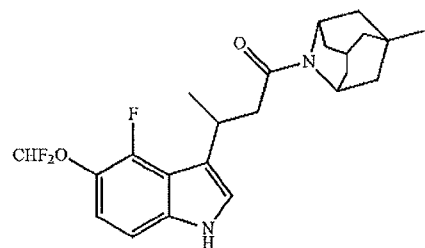


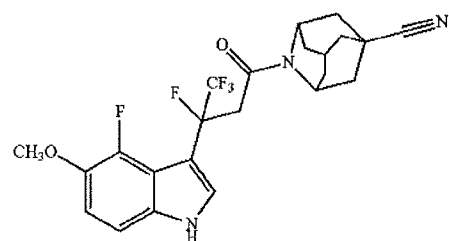
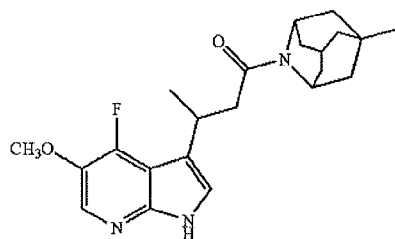
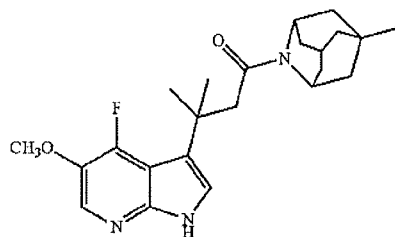
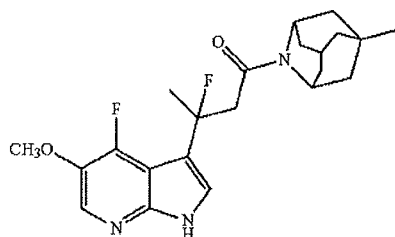
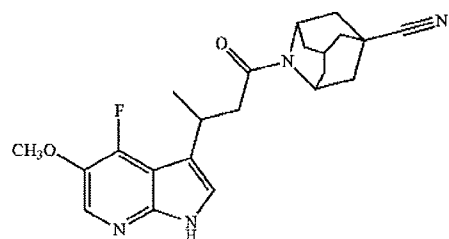
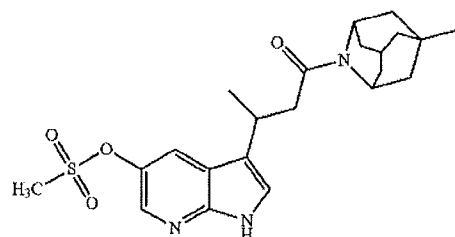


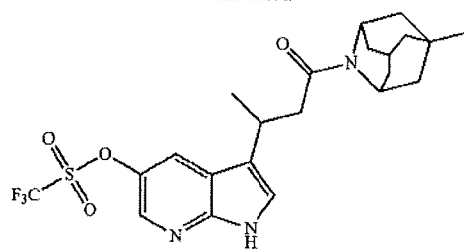
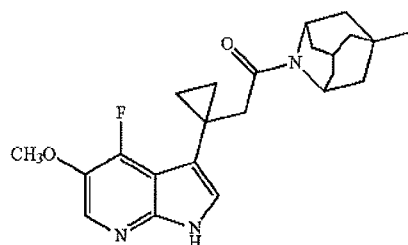
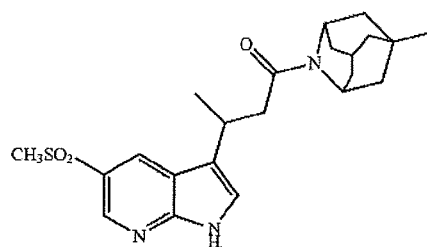
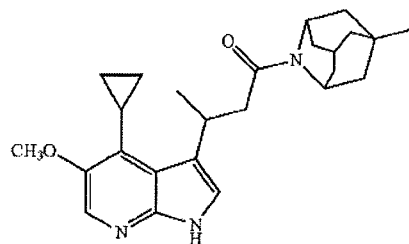
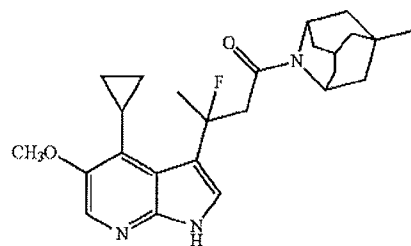
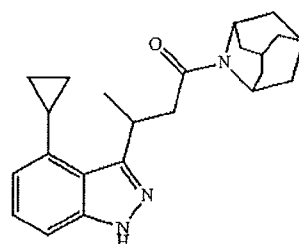


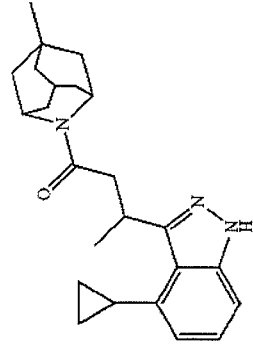
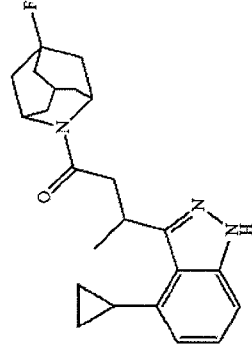
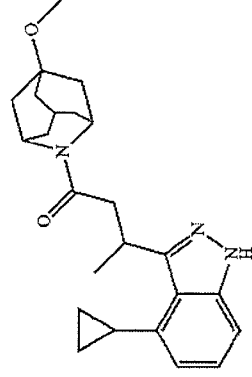
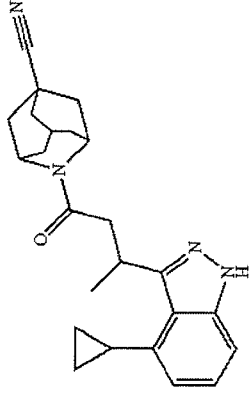
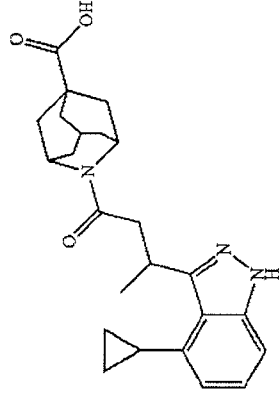
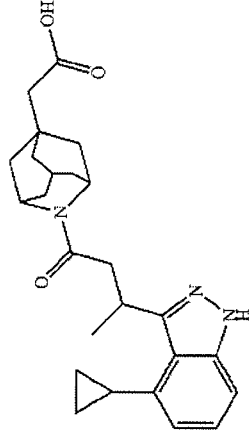


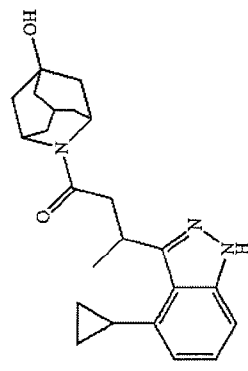
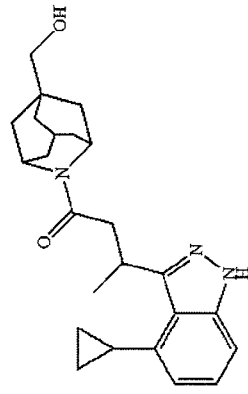
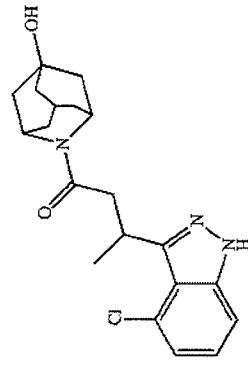
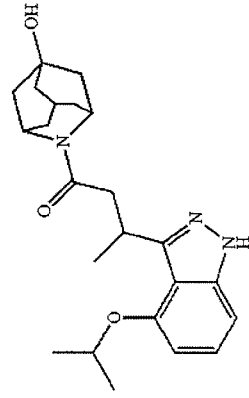
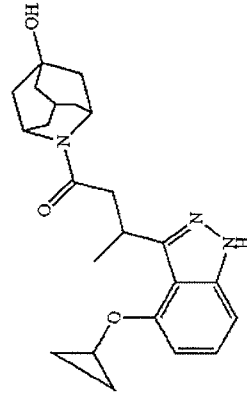
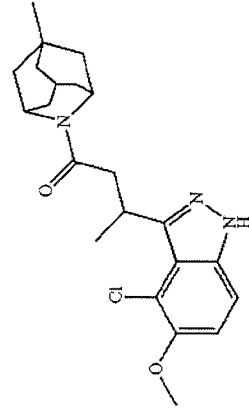


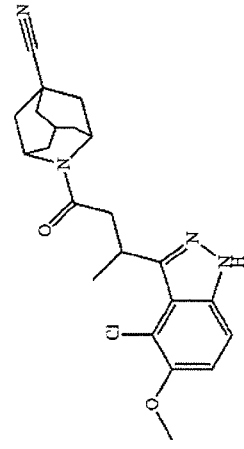
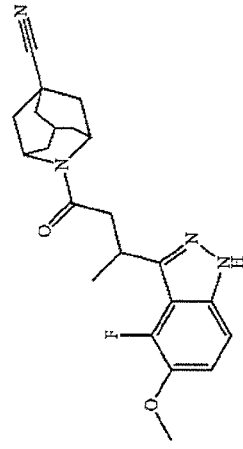
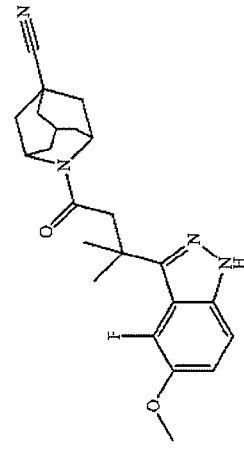
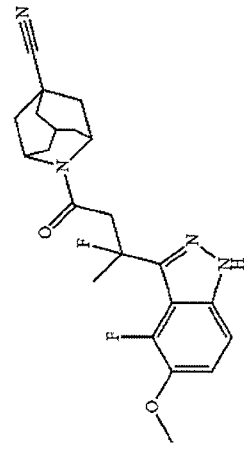
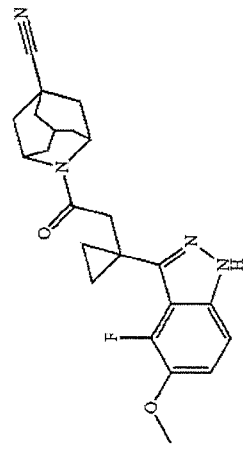
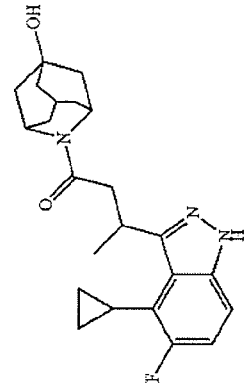


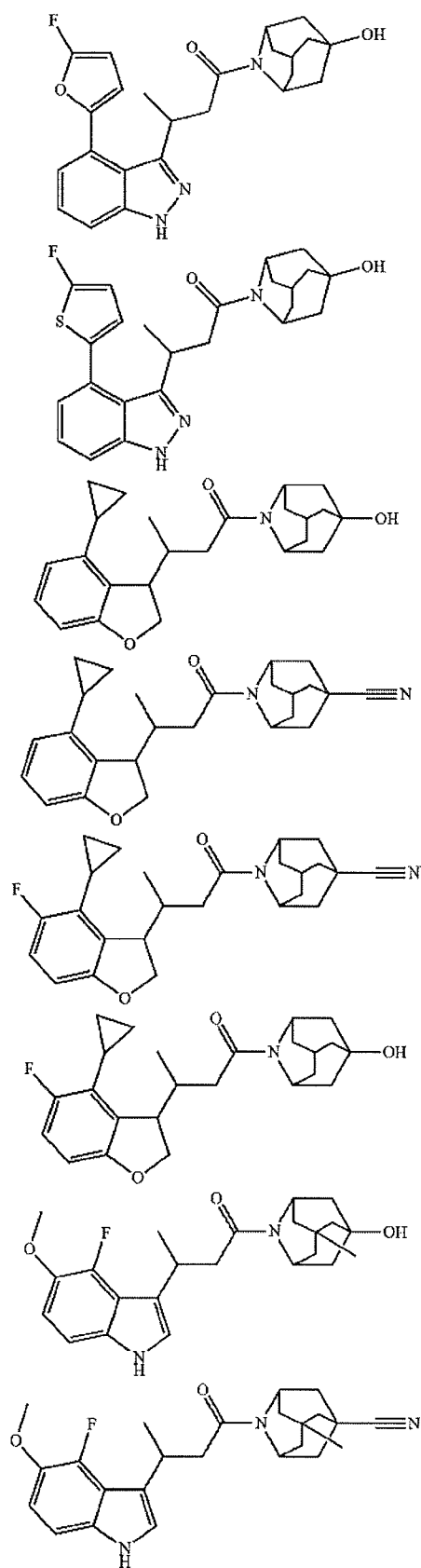


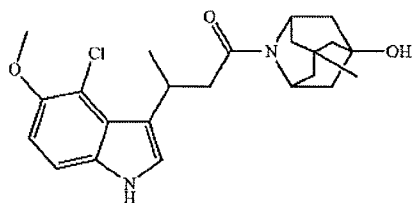
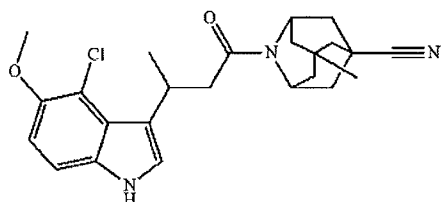
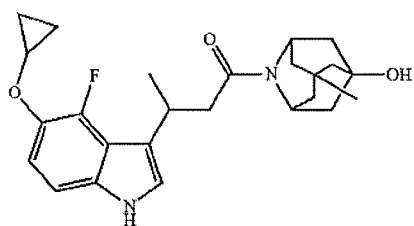
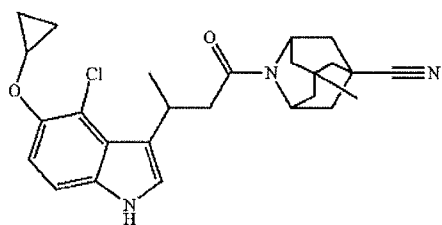
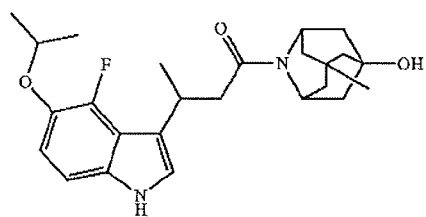
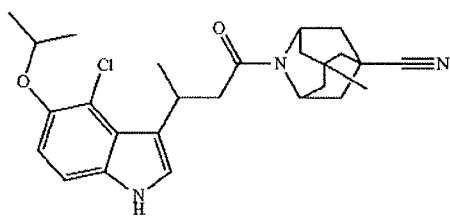
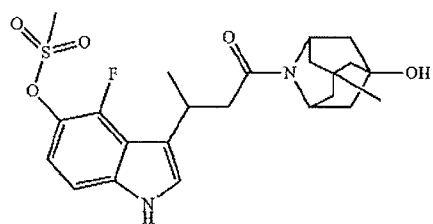


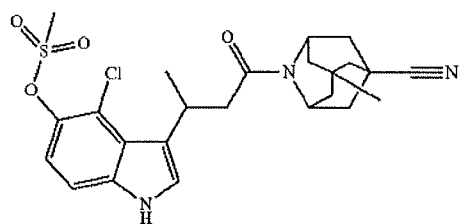
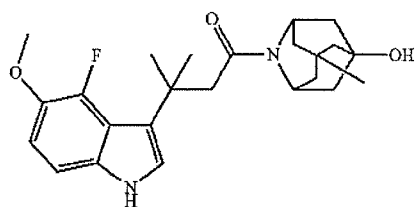
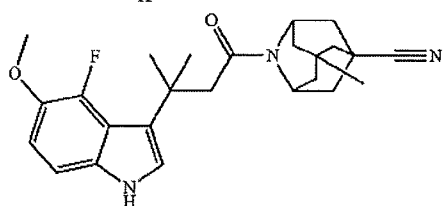
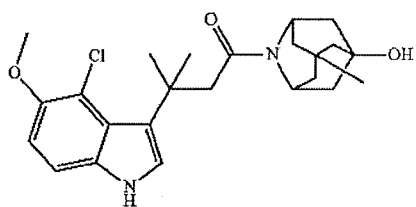
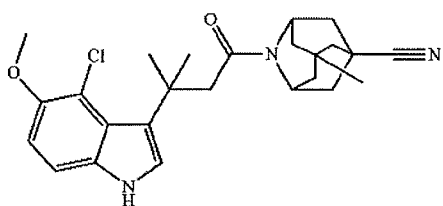
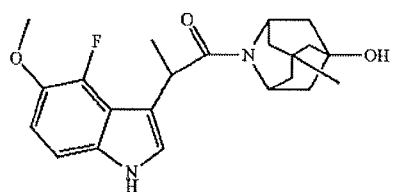
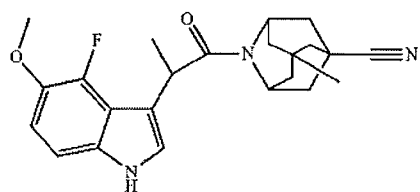
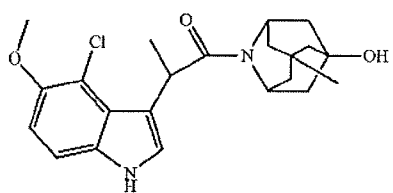


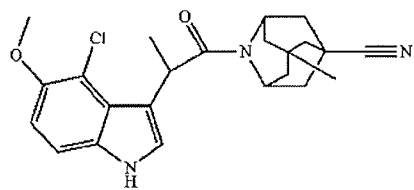
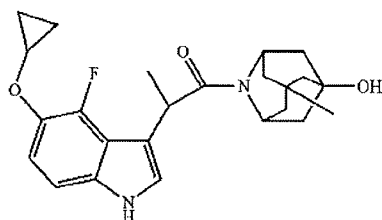
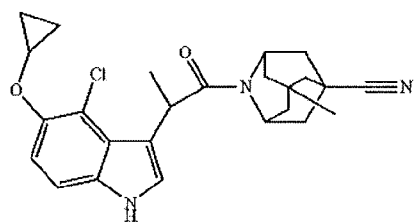
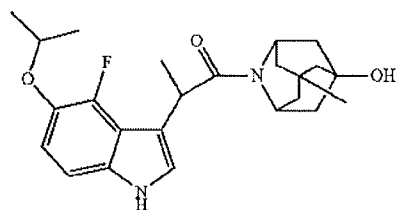
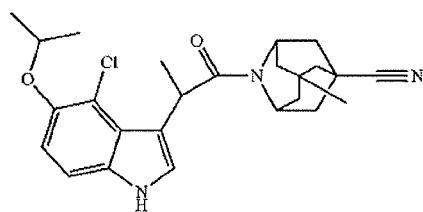
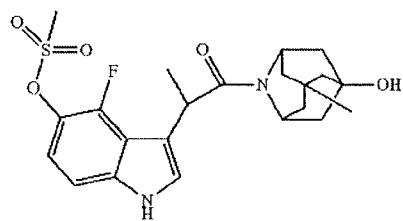
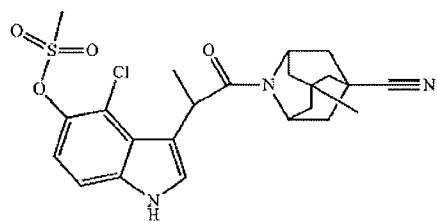


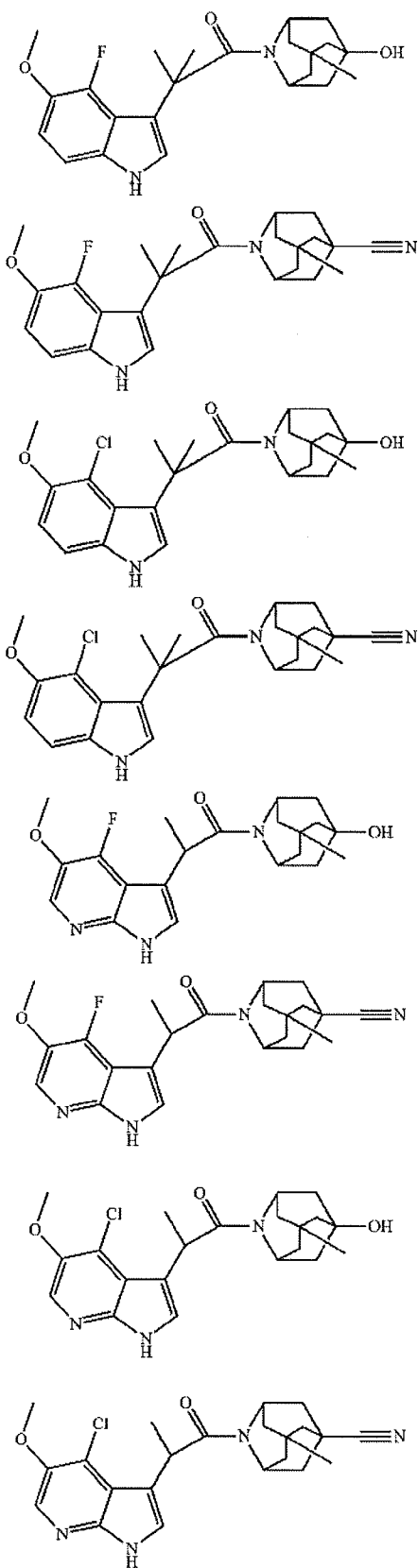


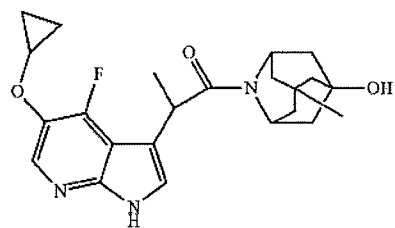
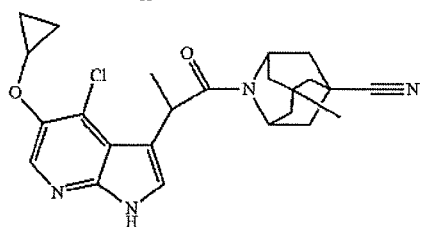
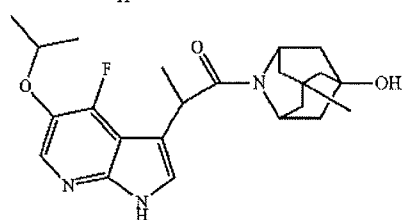
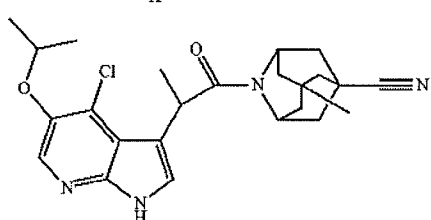
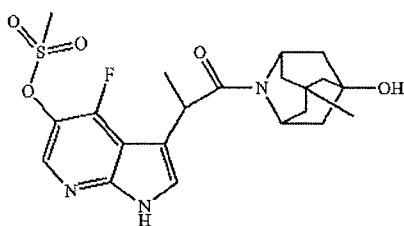
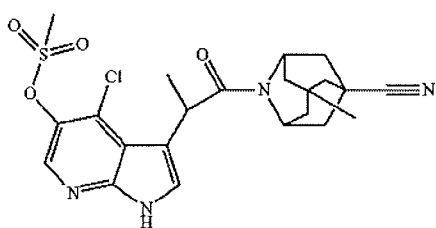
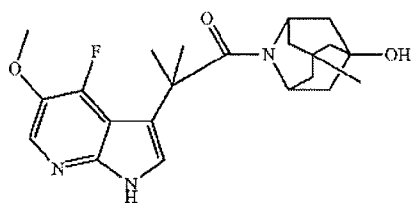


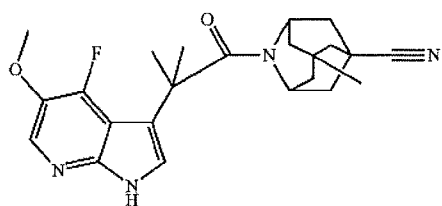
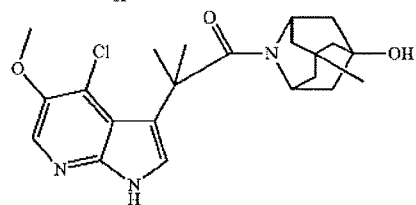
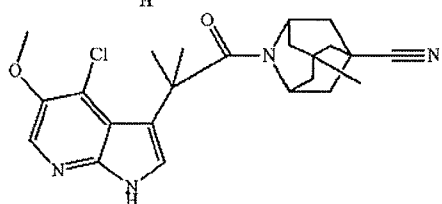
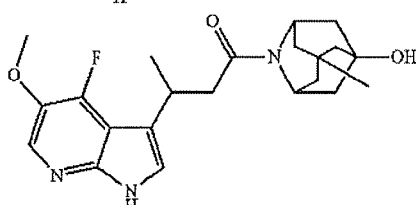
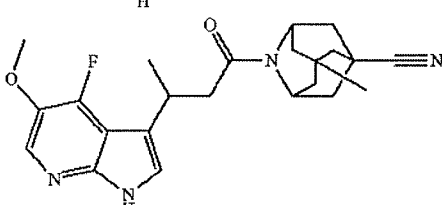
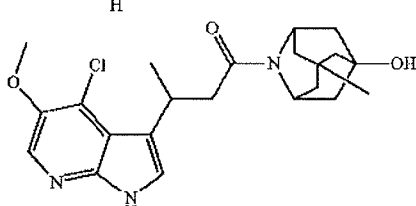
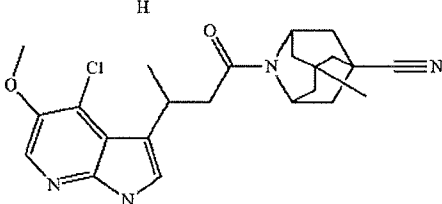
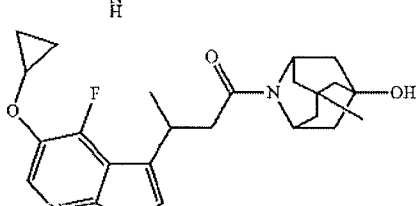


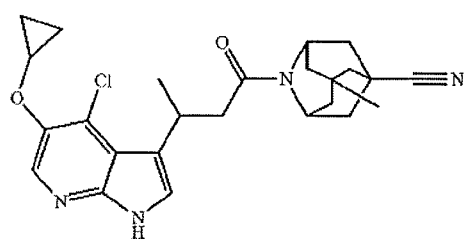
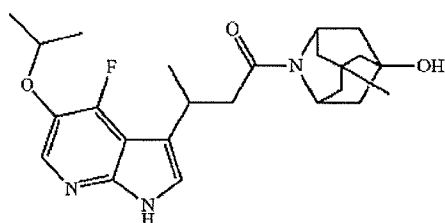
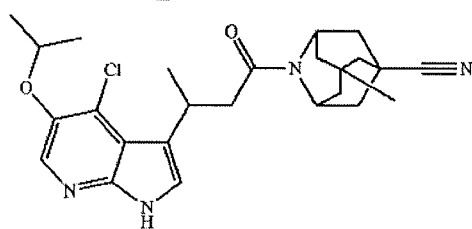
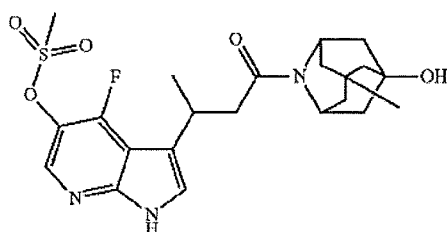
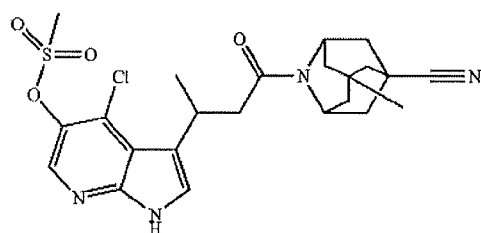
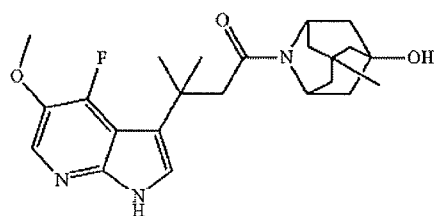
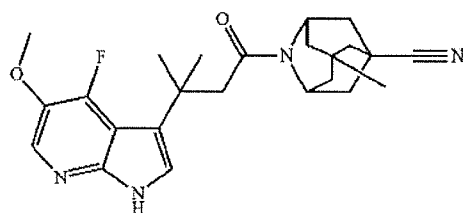


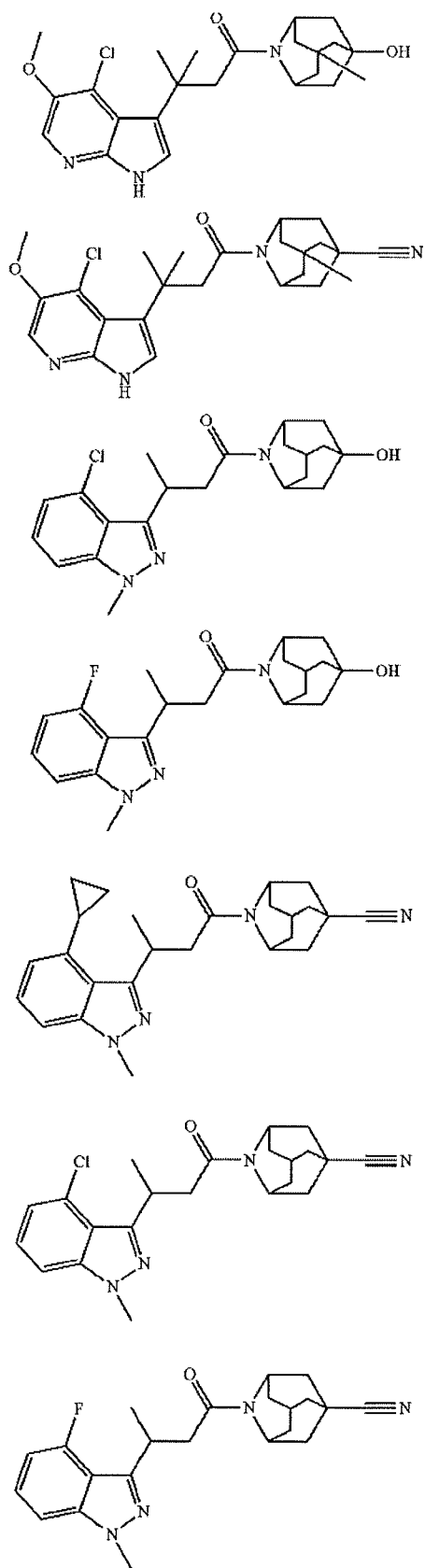


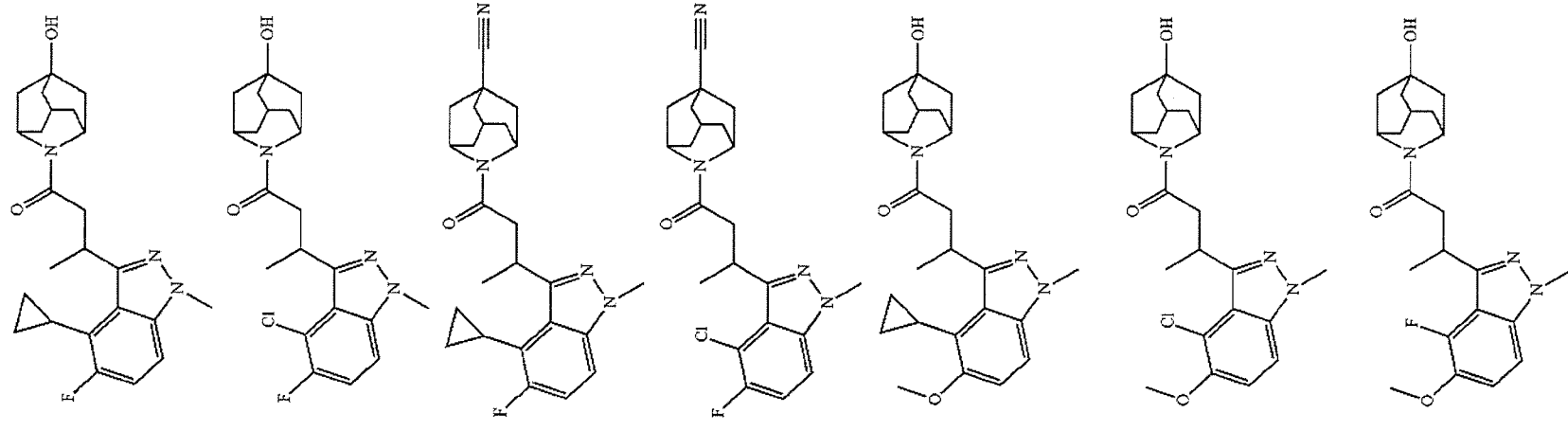


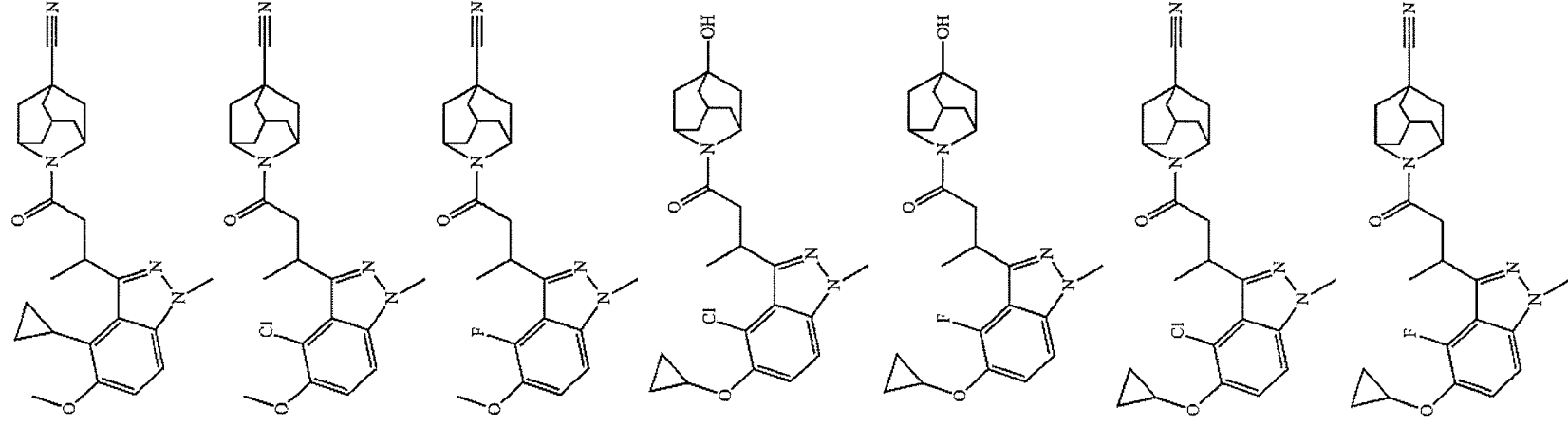


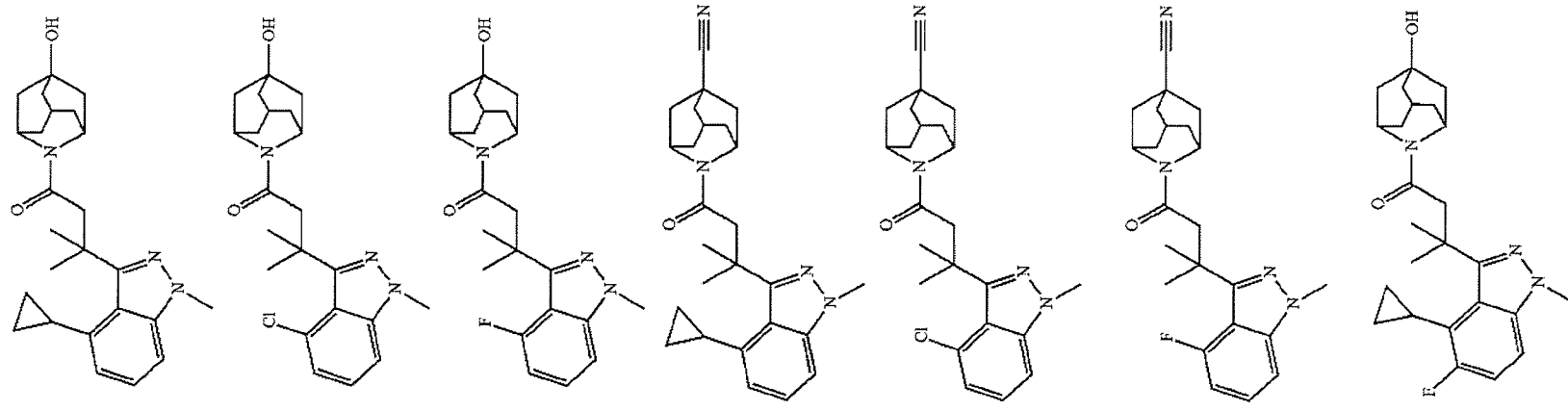


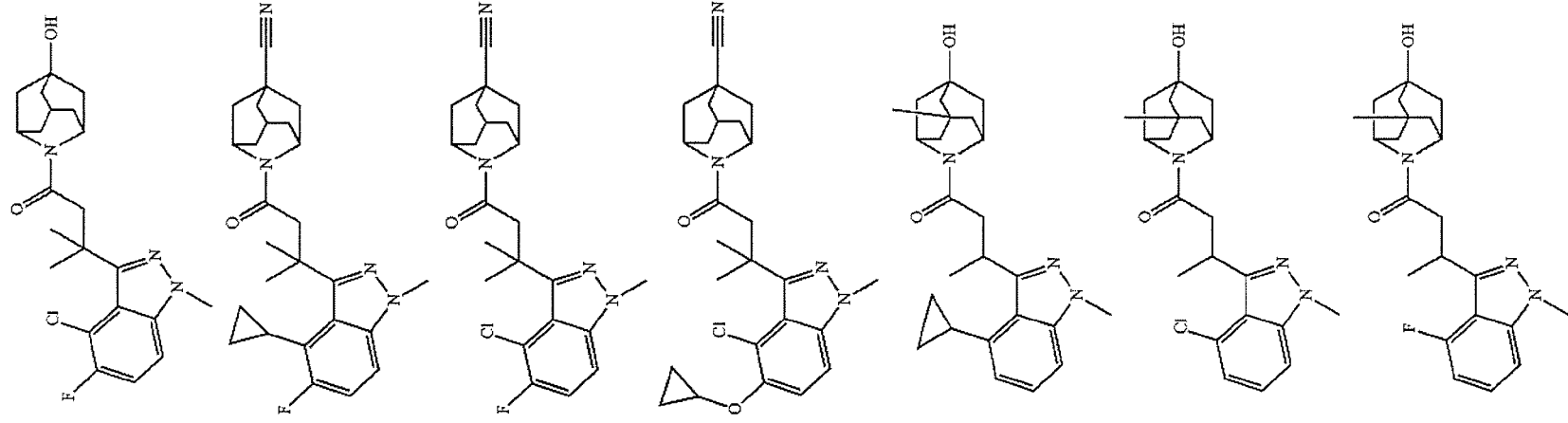


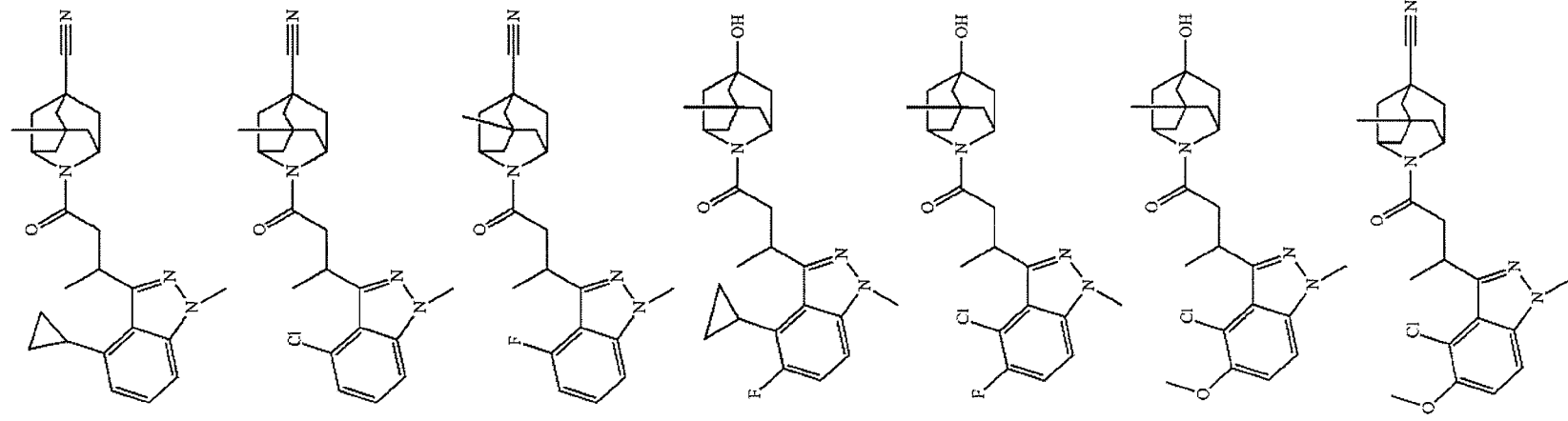


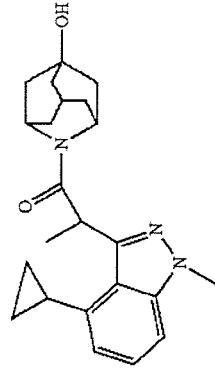
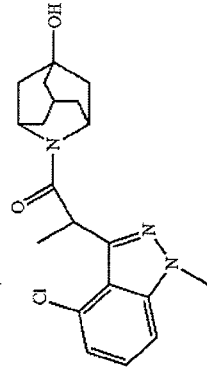
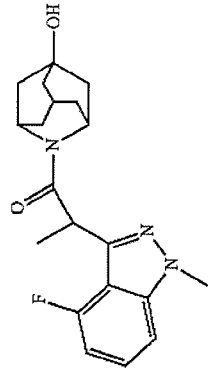
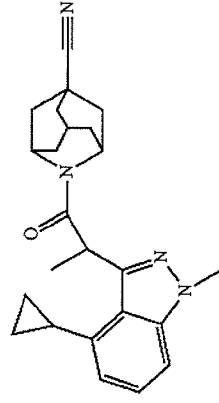
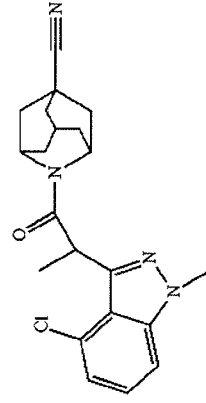
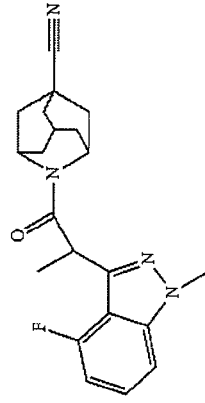
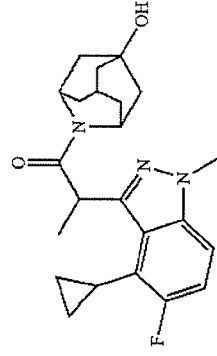


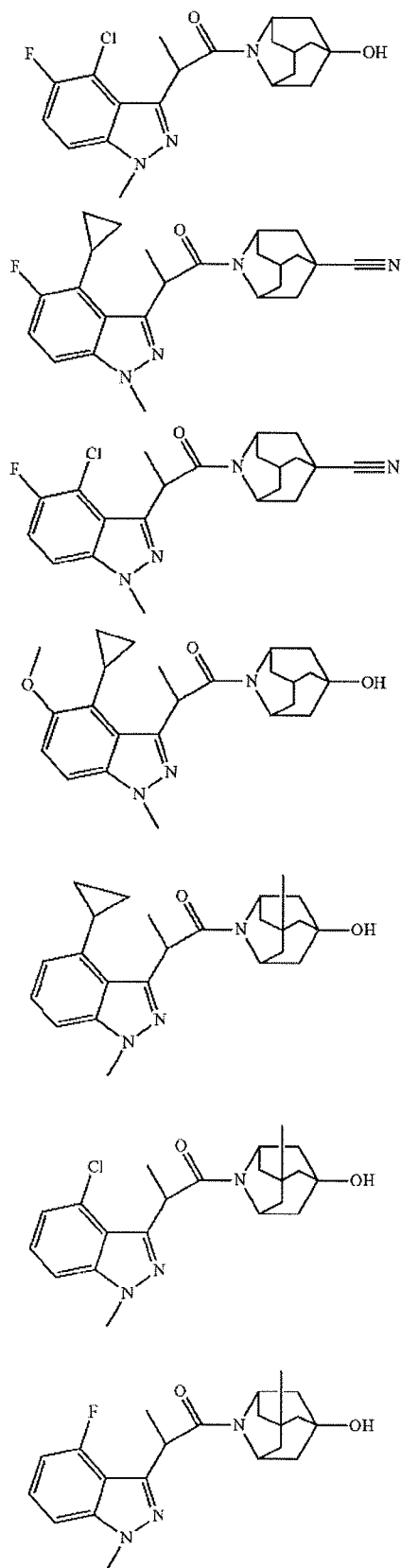


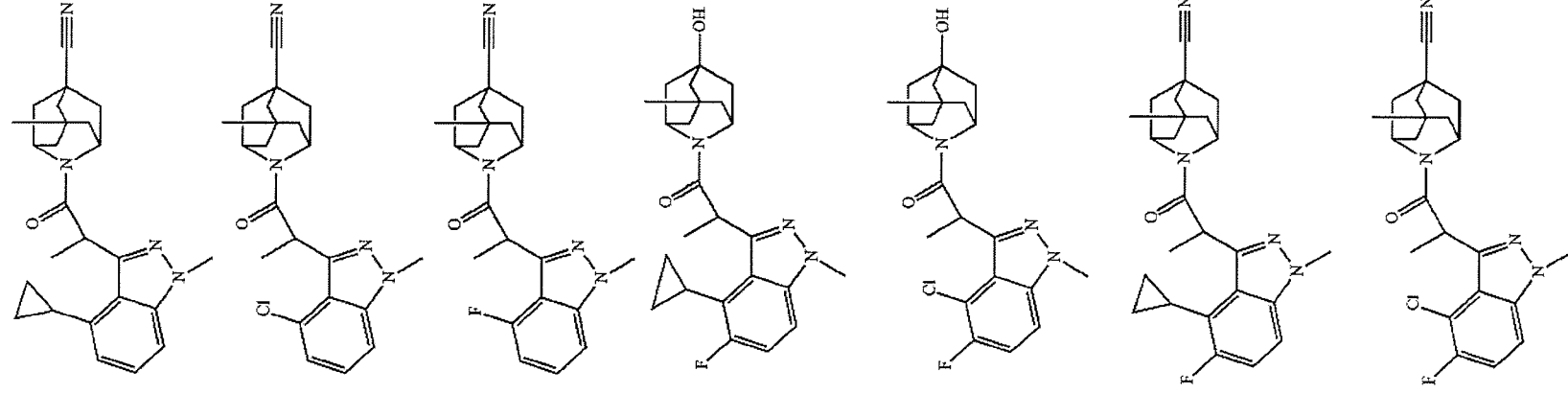


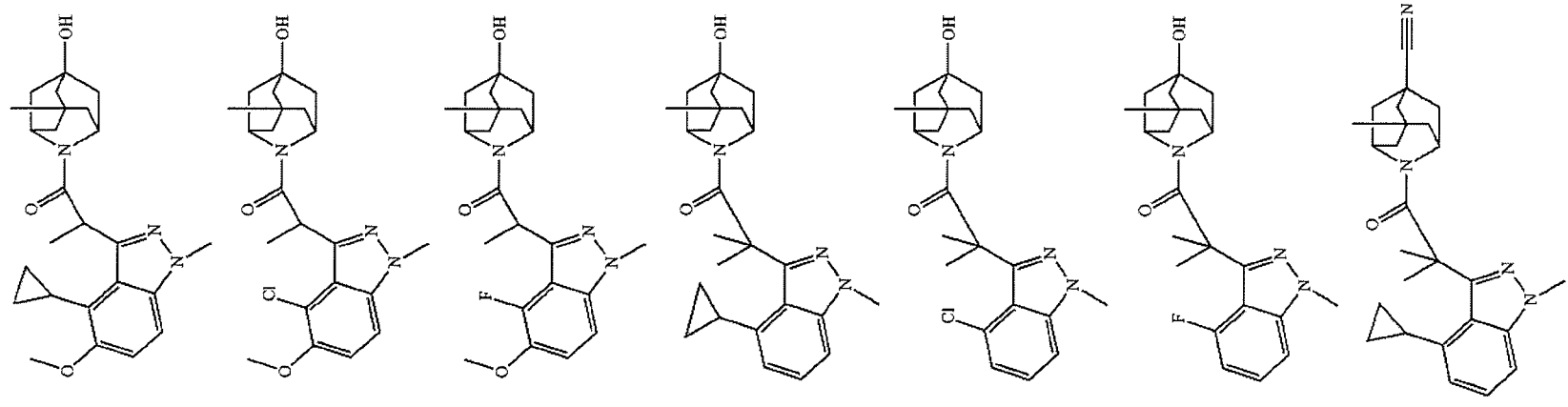


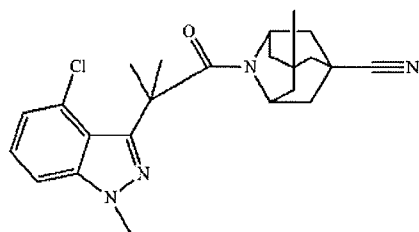
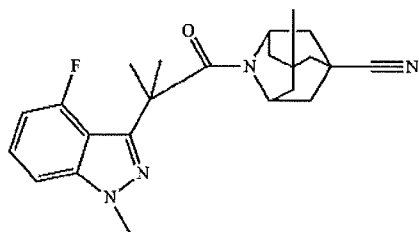
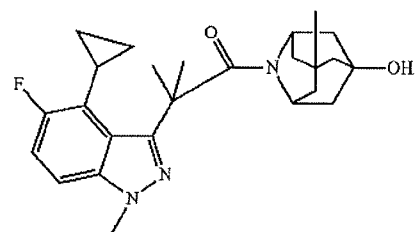
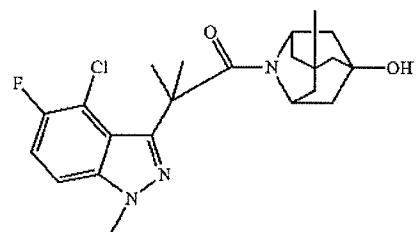
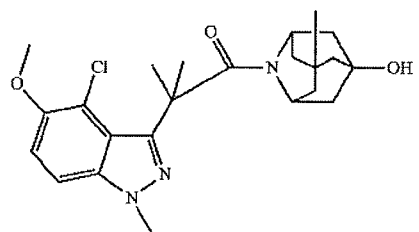
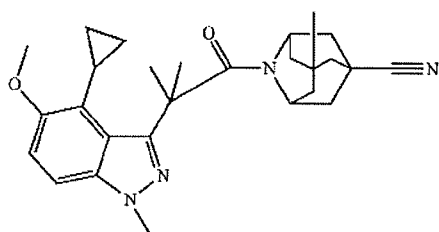
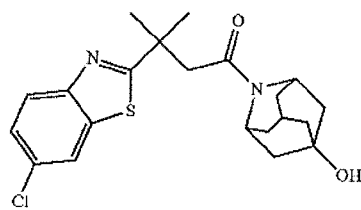


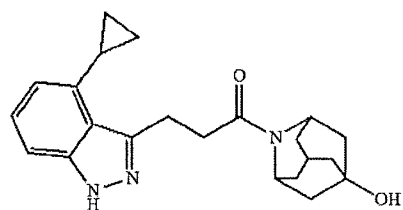
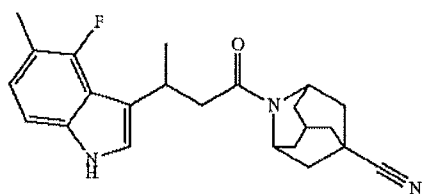
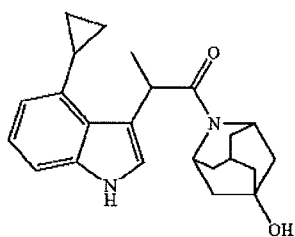
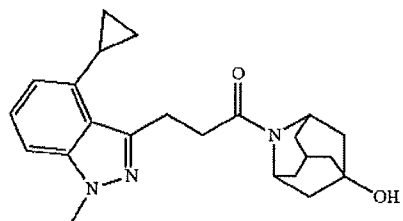
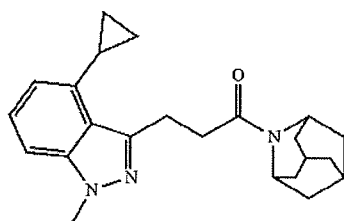
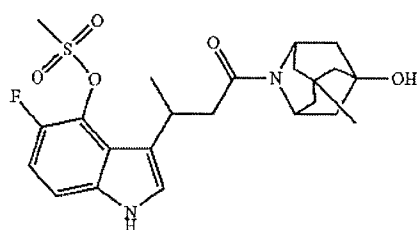
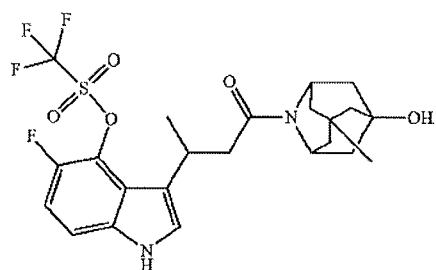


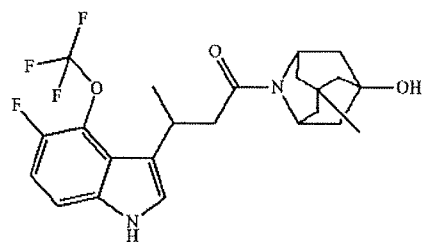
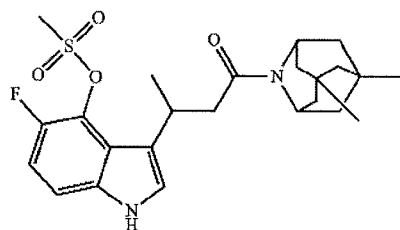
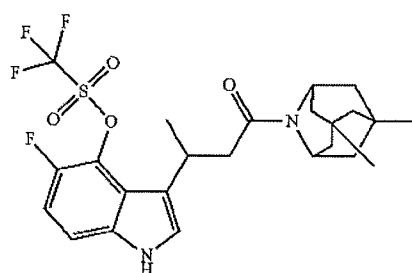
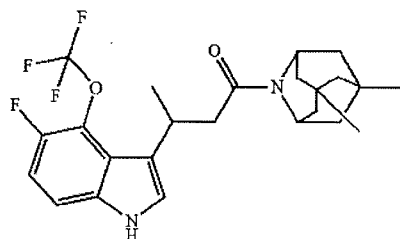
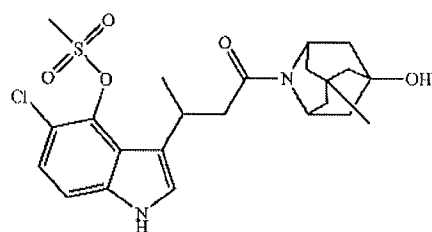
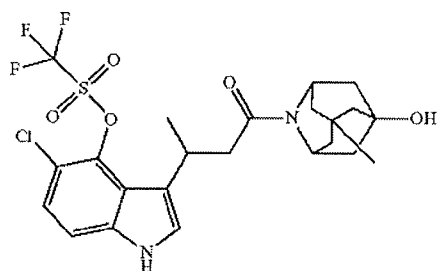


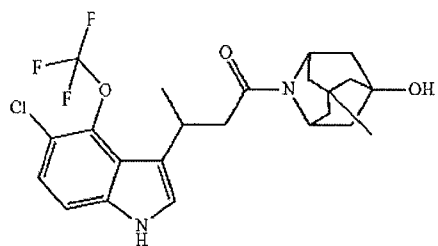
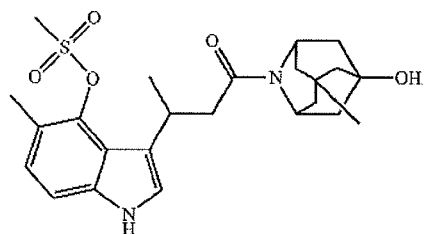
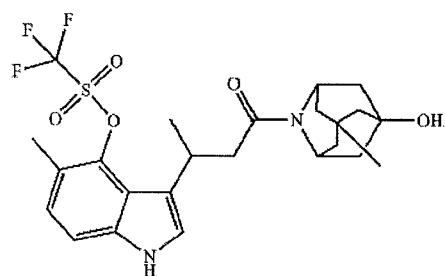
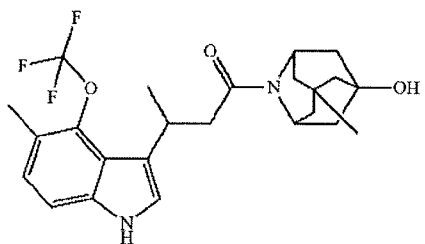
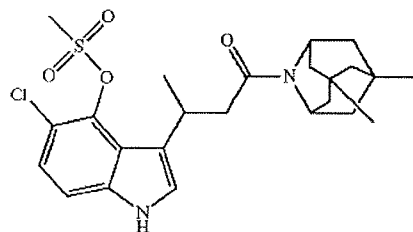
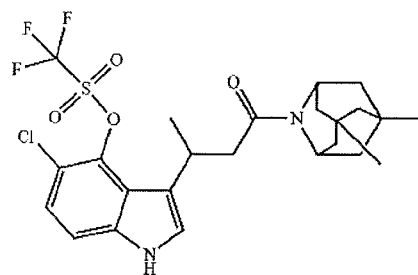


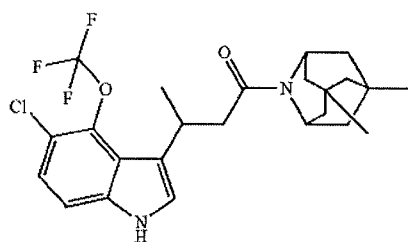
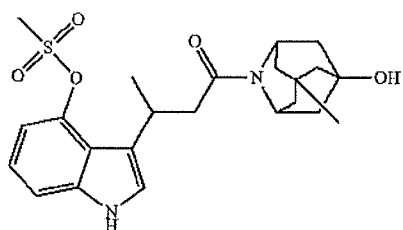
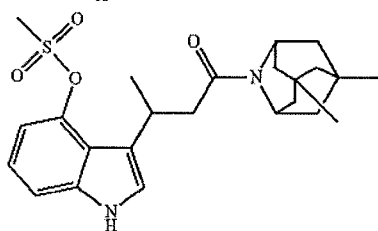
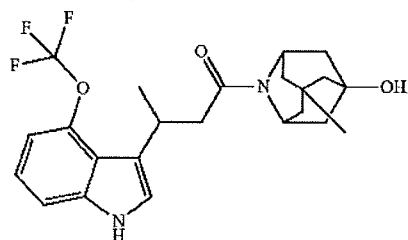
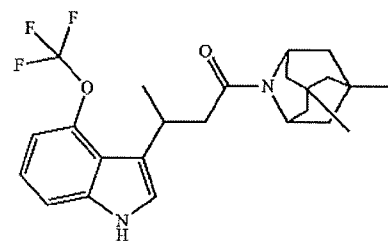
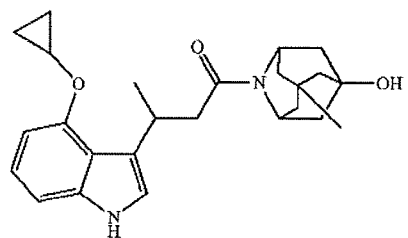
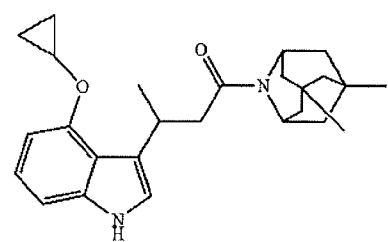


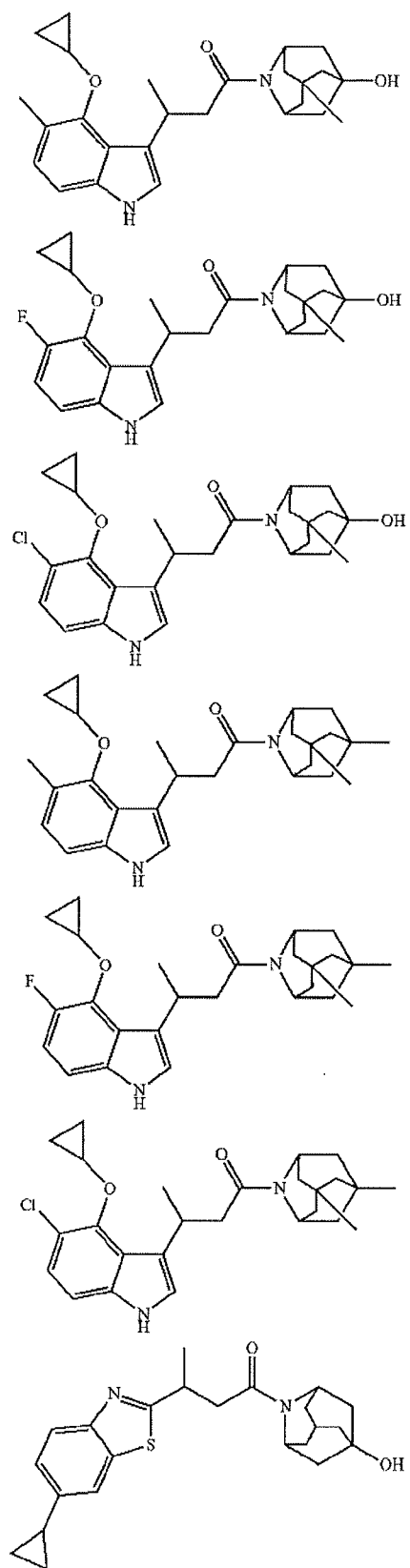


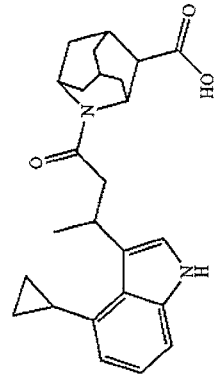
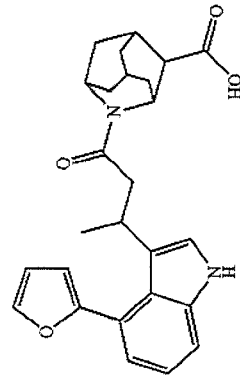
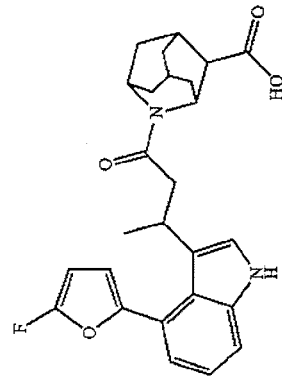
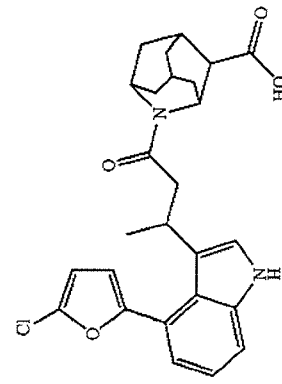
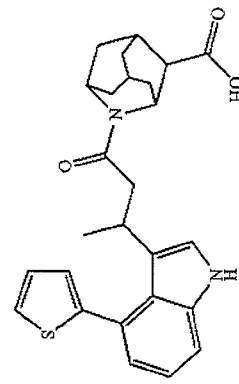
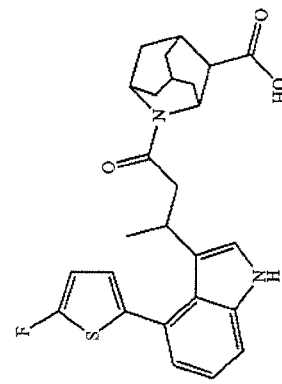


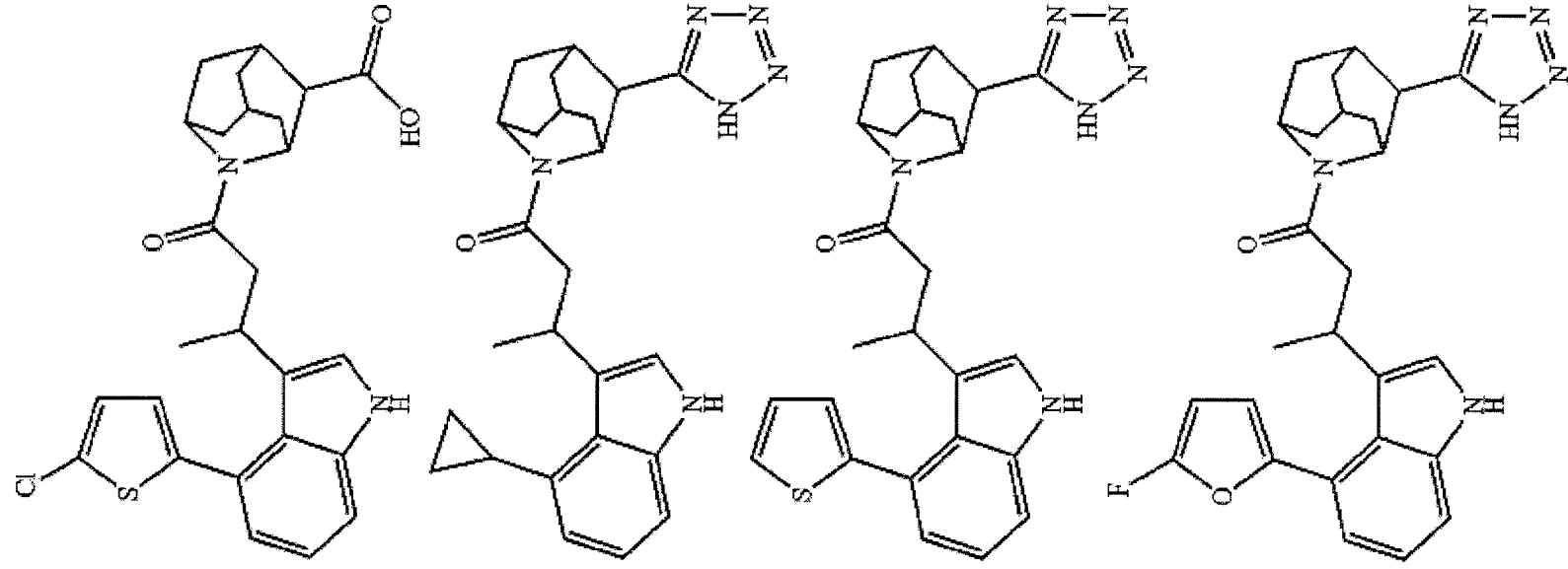


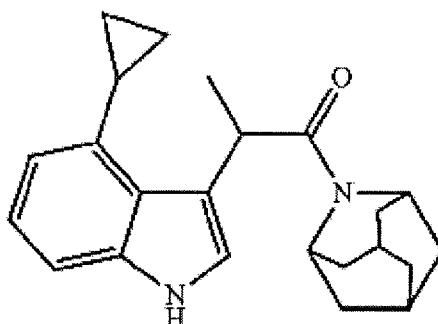












or pharmaceutically acceptable salts and isomers thereof.

11. A pharmaceutical composition including a compound according to claim 1 and a pharmaceutically acceptable diluent, excipient or carrier.

12. A method of treatment of diabetes in a mammal that is treated by inhibition of 11 β HSD1, the method comprising administering an effective amount of a compound according to claim 1.

13. A method according to claim 12 wherein the diabetes is type II diabetes.

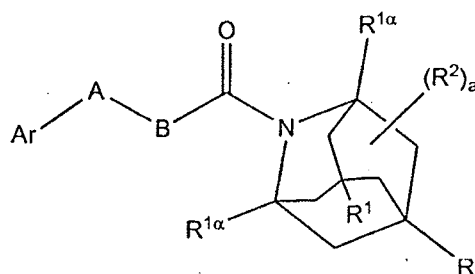
14. The method of claim 12, wherein the compound is administered in combination with an adjuvant.

15. The method of claim 14, wherein the adjuvant is selected from the group consisting of dipeptidyl peptidase-IV (DP-IV) inhibitors; (b) insulin sensitizing agents; (c) insulin and insulin mimetics; (d) sulfonylureas and other insulin secretagogues; (e) alpha-glucosidase inhibitors; (f) GLP-1, GLP-1 analogs, and GLP-1 receptor agonists; and combinations thereof.

16. The method of claim 15, wherein the insulin sensitizing agents are selected from the group consisting of (i) PPAR-gamma-agonists, (ii) PPAR-alpha-agonists, (iii) PPAR-alpha/gamma-dual agonists, (iv) biguanides, and combinations thereof.

Claims:

1. A compound of formula (I):



Formula (I)

wherein:

- each R^1 , $R^{1\alpha}$ and R^2 is independently selected from the group consisting of H,
 10 halogen, OH, NO_2 , CN, SH, NH_2 , CF_3 , OCF_3 , OCH_3 , CH_2OH , $\text{CH}_2\text{CO}_2\text{H}$, $\text{CH}_2\text{CH}_2\text{CO}_2\text{H}$,
 CH_2NH_2 , optionally substituted $\text{C}_1\text{-C}_{12}$ alkyl, optionally substituted $\text{C}_1\text{-C}_{12}$ haloalkyl optionally
 substituted $\text{C}_2\text{-C}_{12}$ alkenyl, optionally substituted $\text{C}_2\text{-C}_{12}$ alkynyl, optionally substituted $\text{C}_2\text{-}$
 C_{12} heteroalkyl, optionally substituted $\text{C}_3\text{-C}_{12}$ cycloalkyl, optionally substituted $\text{C}_3\text{-}$
 C_{12} cycloalkenyl, optionally substituted $\text{C}_2\text{-C}_{12}$ heterocycloalkyl, optionally substituted $\text{C}_2\text{-}$
 15 C_{12} heterocycloalkenyl, optionally substituted $\text{C}_6\text{-C}_{18}$ aryl, optionally substituted $\text{C}_1\text{-}$
 C_{18} heteroaryl, optionally substituted $\text{C}_1\text{-C}_{12}$ alkyloxy, optionally substituted $\text{C}_2\text{-C}_{12}$ alkenyloxy,
 optionally substituted $\text{C}_2\text{-C}_{12}$ alkynyloxy, optionally substituted $\text{C}_2\text{-C}_{10}$ heteroalkyloxy, optionally
 substituted $\text{C}_3\text{-C}_{12}$ cycloalkyloxy, optionally substituted $\text{C}_3\text{-C}_{12}$ cycloalkenyloxy, optionally
 substituted $\text{C}_2\text{-C}_{12}$ heterocycloalkyloxy, optionally substituted $\text{C}_2\text{-C}_{12}$ heterocycloalkenyloxy,
 20 optionally substituted $\text{C}_6\text{-C}_{18}$ aryloxy, optionally substituted $\text{C}_1\text{-C}_{18}$ heteroaryloxy, optionally
 substituted $\text{C}_1\text{-C}_{12}$ alkylamino, SR^3 , SO_3H , $\text{SO}_2\text{NR}^3\text{R}^4$, SO_2R^3 , SONR^3R^4 , SOR^3 , COR^3 ,
 COOH , COOR^3 , CONR^3R^4 , NR^3COR^4 , NR^3COOR^4 , $\text{NR}^3\text{SO}_2\text{R}^4$, $\text{NR}^3\text{CONR}^3\text{R}^4$, and NR^3R^4 ;

- Ar is an optionally substituted $\text{C}_1\text{-C}_{18}$ heteroaryl group or an optionally substituted $\text{C}_2\text{-}$
 25 C_{12} heterocycloalkyl group;

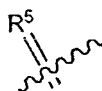
A is selected from the group consisting of S, SO, SO_2 , O, and $-\text{CR}^a\text{R}^b$;

B is a group of the formula $-(\text{CR}^c\text{R}^d)_n$;

wherein each R^a , R^b , R^c and R^d is independently selected from the group consisting of H, halogen, OH, NO_2 , CN, SH, NH_2 , CF_3 , OCF_3 , optionally substituted $\text{C}_1\text{-C}_{12}$ alkyl, optionally substituted $\text{C}_2\text{-C}_{10}$ heteroalkyl, optionally substituted $\text{C}_1\text{-C}_{12}$ haloalkyl, optionally substituted $\text{C}_3\text{-C}_{12}$ cycloalkyl, optionally substituted $\text{C}_6\text{-C}_{18}$ aryl, optionally substituted $\text{C}_1\text{-C}_{18}$ heteroaryl; SR^3 ,
 5 SO_3H , $\text{SO}_2\text{NR}^3\text{R}^4$, SO_2R^3 , SONR^3R^4 , SOR^3 , COR^3 , COOH , COOR^3 , CONR^3R^4 , NR^3COR^4 ,
 NR^3COOR^4 , $\text{NR}^3\text{SO}_2\text{R}^4$, $\text{NR}^3\text{CONR}^3\text{R}^4$, NR^3R^4 ;

or any two R^a , R^b , R^c and R^d on the same carbon atom when taken together may form a substituent of the formula:

10



wherein each R^3 and R^4 is independently selected from the group consisting of H, optionally substituted $\text{C}_1\text{-C}_{12}$ alkyl, optionally substituted $\text{C}_2\text{-C}_{10}$ heteroalkyl, optionally substituted $\text{C}_1\text{-C}_{12}$ haloalkyl, optionally substituted $\text{C}_3\text{-C}_{12}$ cycloalkyl, optionally substituted $\text{C}_6\text{-C}_{18}$ aryl, and optionally substituted $\text{C}_1\text{-C}_{18}$ heteroaryl;

15

R^5 is selected from the group consisting of O, S, and NR^6 ;

20

R^6 is selected from the group consisting of H, OR^7 , optionally substituted $\text{C}_1\text{-C}_{12}$ alkyl, optionally substituted $\text{C}_1\text{-C}_{12}$ haloalkyl, optionally substituted $\text{C}_2\text{-C}_{12}$ alkenyl, optionally substituted $\text{C}_2\text{-C}_{12}$ alkynyl, optionally substituted $\text{C}_1\text{-C}_{12}$ alkyloxy, optionally substituted $\text{C}_1\text{-C}_{12}$ haloalkyloxy, optionally substituted $\text{C}_2\text{-C}_{10}$ heteroalkyl, optionally substituted $\text{C}_3\text{-C}_{12}$ cycloalkyl, optionally substituted $\text{C}_3\text{-C}_{12}$ cycloalkenyl, optionally substituted $\text{C}_2\text{-C}_{12}$ heterocycloalkyl, optionally substituted $\text{C}_2\text{-C}_{12}$ heterocycloalkenyl, optionally substituted $\text{C}_6\text{-C}_{18}$ aryl, and optionally substituted $\text{C}_1\text{-C}_{18}$ heteroaryl;

25

R^7 is selected from the group consisting of H, optionally substituted $\text{C}_1\text{-C}_{12}$ alkyl, optionally substituted $\text{C}_2\text{-C}_{10}$ heteroalkyl, optionally substituted $\text{C}_3\text{-C}_{12}$ cycloalkyl, optionally substituted $\text{C}_6\text{-C}_{18}$ aryl, and optionally substituted $\text{C}_1\text{-C}_{18}$ heteroaryl;

30

or any two or more R^a , R^b , R^c and R^d may join together to form a multiple bond between adjacent carbon atoms such as a double or triple bond, or a cyclic moiety connecting the carbon atoms to which they are attached;

35

n is an integer selected from the group consisting of 0, 1, 2, 3, and 4;

a is an integer selected from the group consisting of 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

or a pharmaceutically acceptable salt, N-oxide, or prodrug thereof.

2. A compound according to claim 1 wherein B is CH₂.

3. A compound according to claim 1 or 2 wherein A is CR^aR^b.

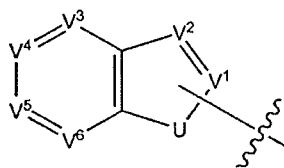
4. A compound according to claim 3 wherein R^a and R^b are different.

5. A compound according to claim 4 wherein one of R^a and R^b is H and the other is optionally substituted alkyl.

6. A compound according to claim 5 wherein R^b is H and R^a is optionally substituted alkyl.

7. A compound according to claim 6 wherein R^a is selected from the group consisting of methyl, ethyl, propyl, isopropyl and butyl.

8. A compound according to any one of claims 1 to 6 wherein Ar is a group of the formula:



wherein each V¹, V², V³, V⁴, V⁵ and V⁶ is independently selected from the group consisting of N and CR⁸;

U is selected from the group consisting of NR⁹, O, S and CR⁹₂,

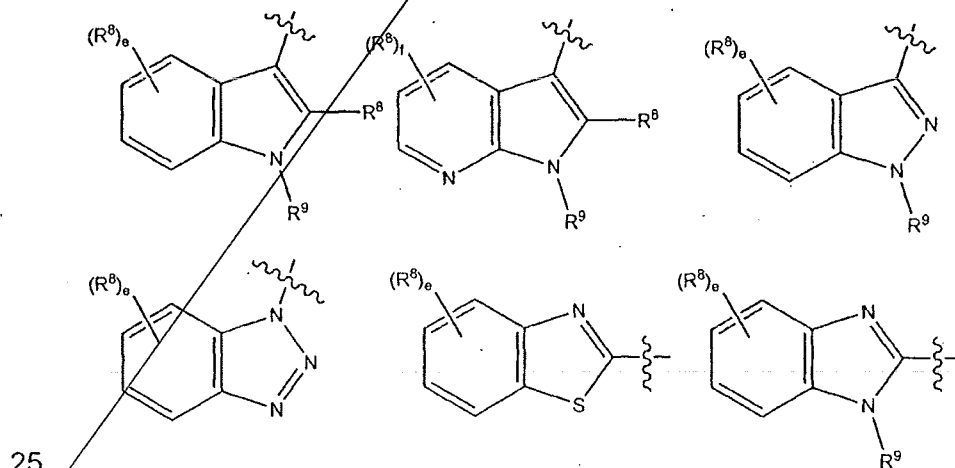
wherein each R⁸ is independently selected from the group consisting of H, halogen, OH, NO₂, CN, SH, NH₂, CF₃, OCF₃, optionally substituted C₁-C₁₂alkyl, optionally substituted C₁-C₁₂haloalkyl, optionally substituted C₂-C₁₂alkenyl, optionally substituted C₂-C₁₂alkynyl, optionally substituted C₂-C₁₂heteroalkyl, optionally substituted C₃-C₁₂cycloalkyl, optionally

substituted C₃-C₁₂cycloalkenyl, optionally substituted C₂-C₁₂heterocycloalkyl, optionally substituted C₂-C₁₂heterocycloalkenyl, optionally substituted C₆-C₁₈aryl, optionally substituted C₁-C₁₈heteroaryl, optionally substituted C₁-C₁₂alkyloxy, optionally substituted C₂-C₁₂alkenyloxy, optionally substituted C₂-C₁₂alkynyloxy, optionally substituted C₂-C₁₀heteroalkyloxy, optionally substituted C₃-C₁₂cycloalkyloxy, optionally substituted C₃-C₁₂cycloalkenyloxy, optionally substituted C₂-C₁₂heterocycloalkyloxy, optionally substituted C₂-C₁₂heterocycloalkenyloxy, optionally substituted C₆-C₁₈aryloxy, optionally substituted C₁-C₁₈heteroaryloxy, optionally substituted C₁-C₁₂alkylamino, SR¹⁰, SO₃H, SO₂NR¹⁰R¹¹, SO₂R¹⁰, OSO₂R¹⁰, SONR¹⁰R¹¹, SOR¹⁰, COR¹⁰, COOH, COOR¹⁰, CONR¹⁰R¹¹, NR¹⁰COR¹¹, NR¹⁰COOR¹¹, NR¹⁰SO₂R¹¹, NR¹⁰CONR¹⁰R¹¹, and NR¹⁰R¹¹;

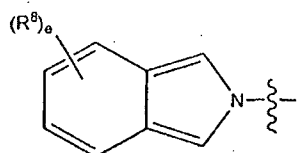
wherein R⁹ is selected from the group consisting of H, optionally substituted C₁-C₁₂alkyl, optionally substituted C₂-C₁₂alkenyl, optionally substituted C₂-C₁₂alkynyl, optionally substituted C₂-C₁₂heteroalkyl, optionally substituted C₃-C₁₂cycloalkyl, optionally substituted C₂-C₁₂heterocycloalkyl, optionally substituted C₆-C₁₈aryl, optionally substituted C₁-C₁₈heteroaryl, SO₃H, SO₂NR¹⁰R¹¹, SO₂R¹⁰, SONR¹⁰R¹¹, SOR¹⁰, COR¹⁰, COOH, COOR¹⁰, and CONR¹⁰R¹¹;

wherein each R¹⁰ and R¹¹ is independently selected from the group consisting of H, optionally substituted C₁-C₁₂alkyl, optionally substituted C₂-C₁₀heteroalkyl, optionally substituted C₁-C₁₂haloalkyl, optionally substituted C₃-C₁₂cycloalkyl, optionally substituted C₆-C₁₈aryl, and optionally substituted C₁-C₁₈heteroaryl.

9. A compound according to claim 8 wherein Ar is selected from the group consisting of:



and



wherein R^8 and R^9 are as defined in claim 8;

5 e is an integer selected from the group consisting of 0, 1, 2, 3, and 4;

f is an integer selected the group consisting of 0, 1, 2, and 3.

10. A compound according to claim 9 wherein the R^8 substituent is located in the 4 or the
10 5 position of the six membered ring.

11. A compound according to claim 9 or 10 wherein each R^8 is independently selected
from the group consisting of CH_3 , CH_2CH_3 , $CH_2CH_2CH_3$, $CH(CH_3)_2$, $(CH_2)_3CH_3$, Cl, Br, F, I,
OH, NO_2 , NH_2 , CN, SO_3H , OCH_3 , $OCH_2CH_2CH_3$, CF_3 , and OCF_3 .

15

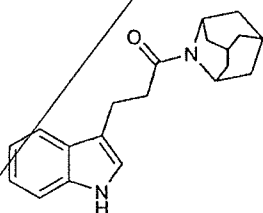
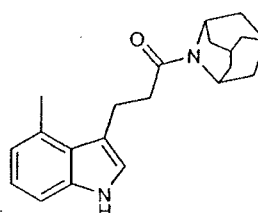
12. A compound according to any one of claims 1 to 11 wherein a is 0.

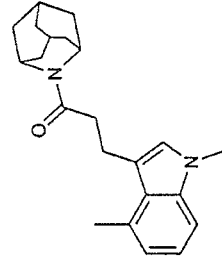
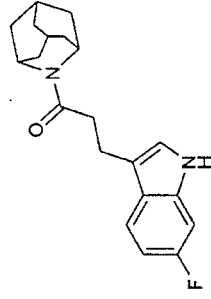
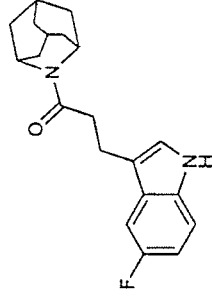
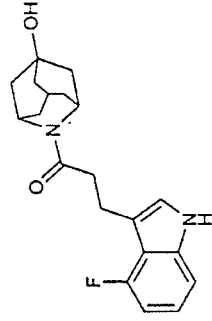
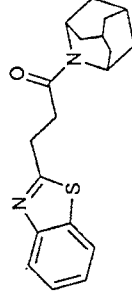
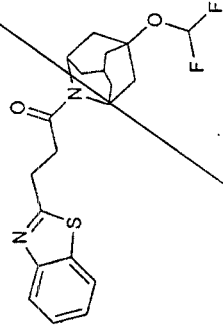
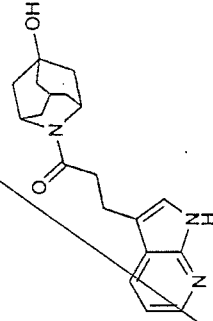
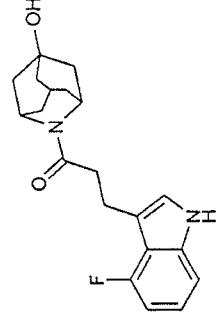
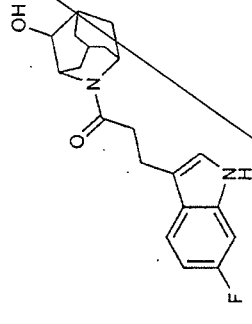
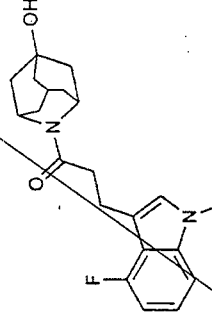
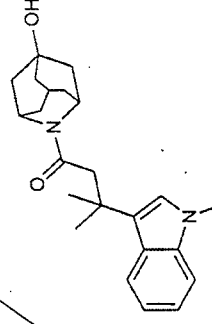
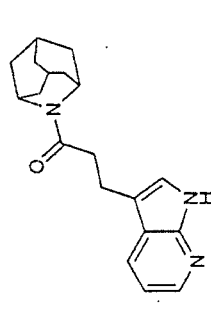
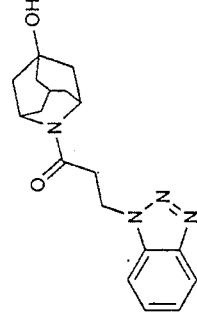
13. A compound according to any one of claims 1 to 12 wherein each R^{1a} is H.

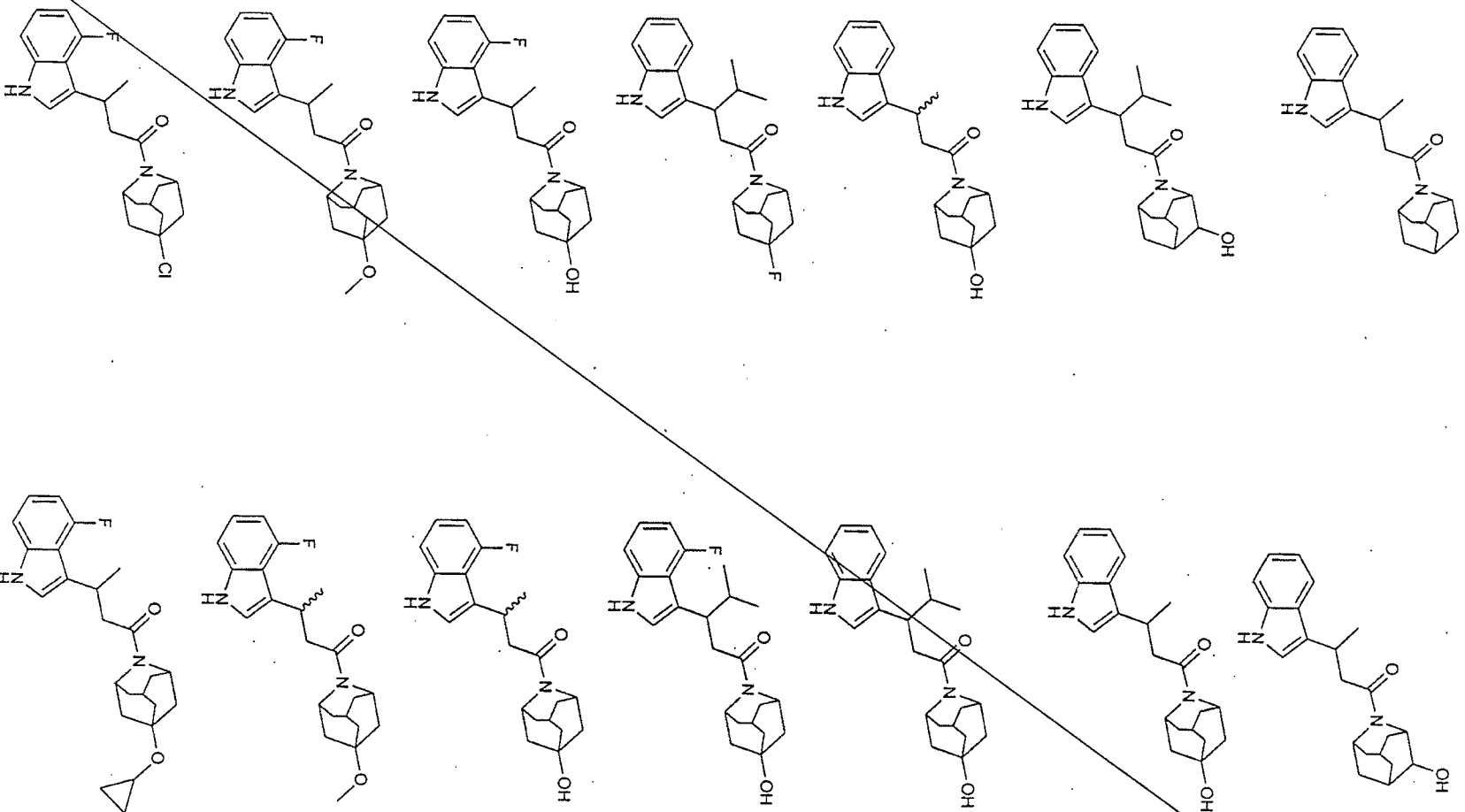
20 14. A compound according to any one of claims 1 to 13 wherein each R^1 is independently
selected from the group consisting of H, OH, F, Cl, Br, CO_2H , $CONH_2$, CH_2OH , CN, OCH_3 ,
and $OCHF_2$.

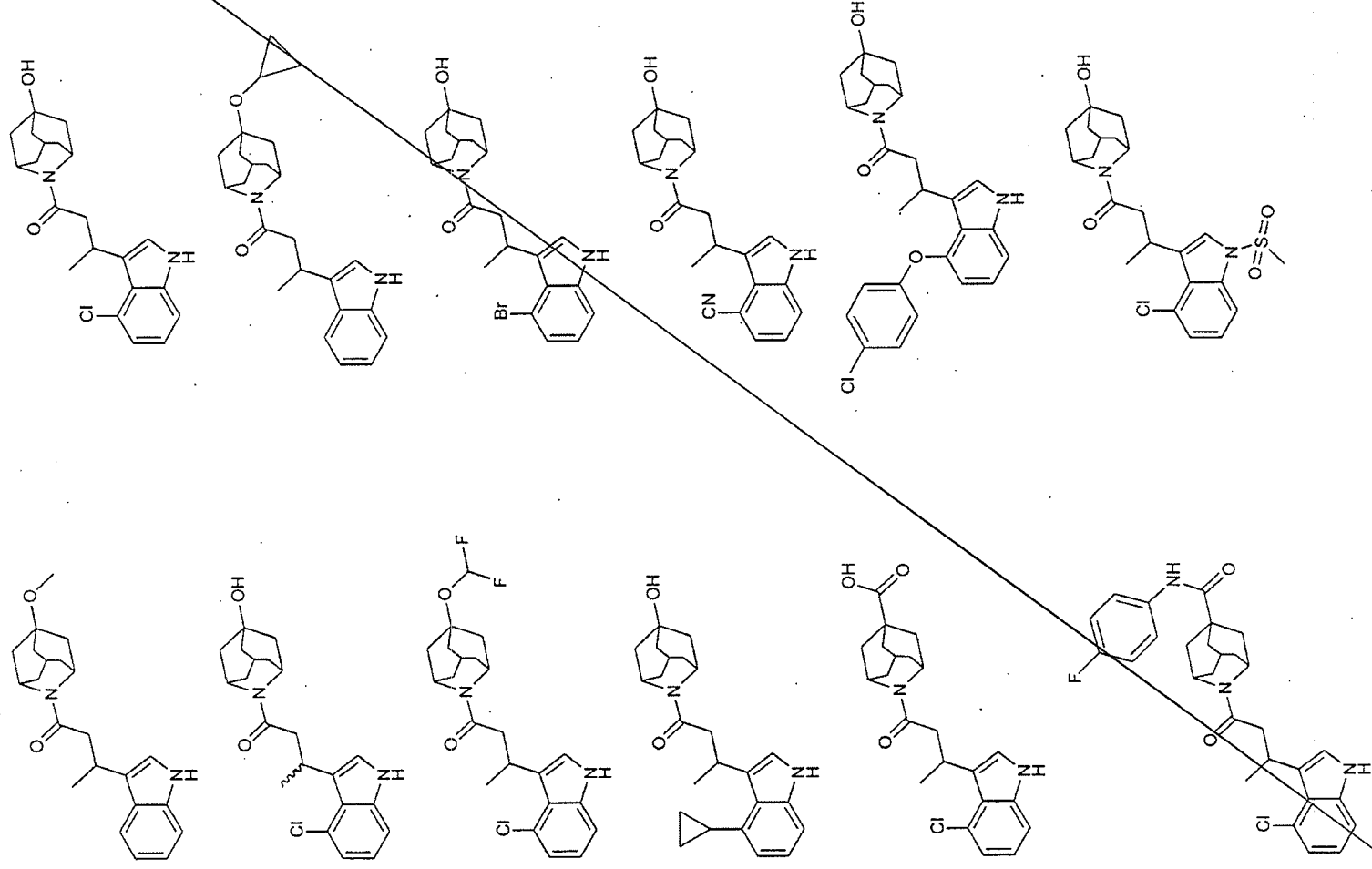
15. A compound according to any one of claims 1 to 14 wherein one R^1 is H and the other
25 R^1 is OH.

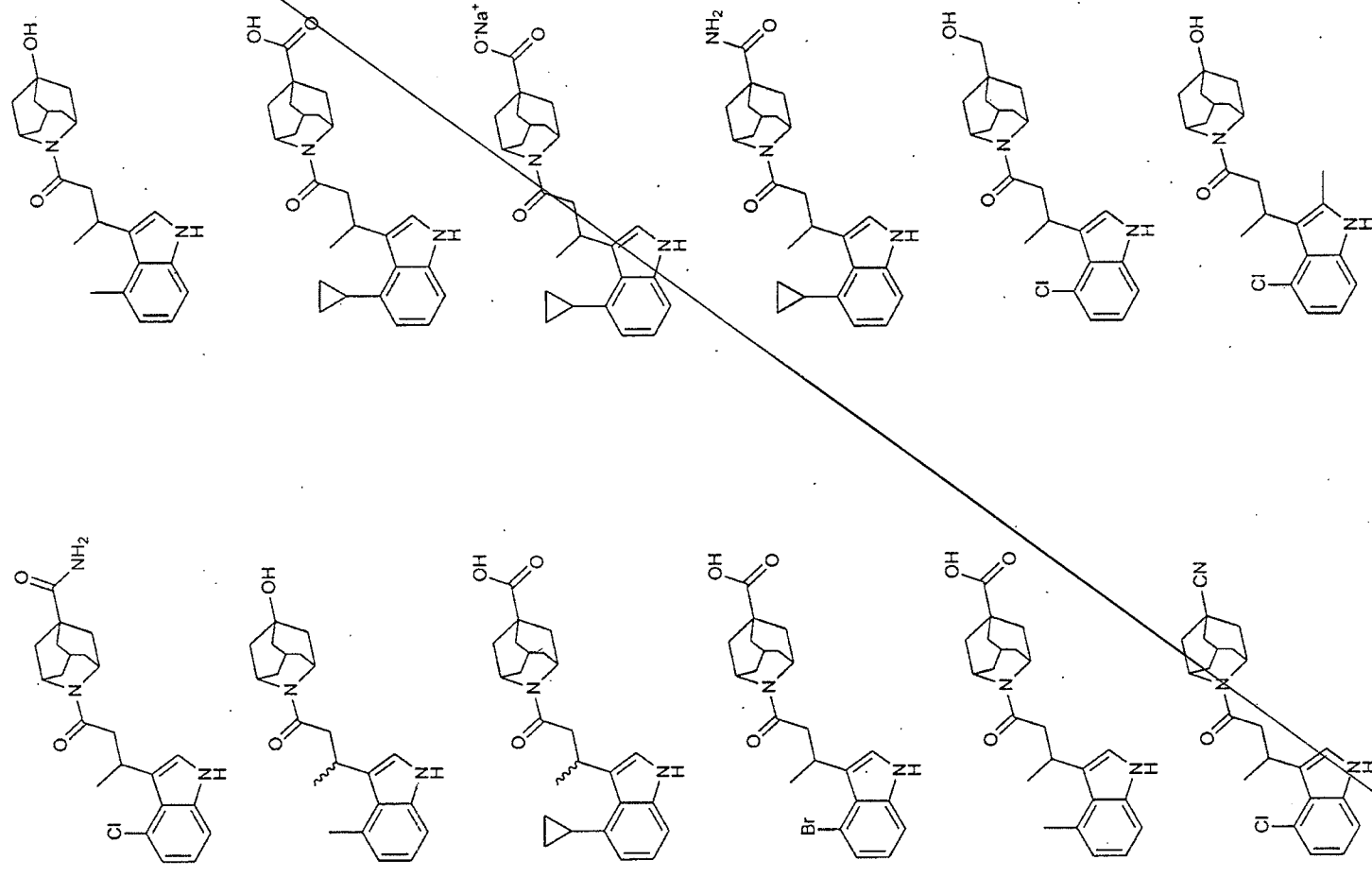
16. A compound according to claim 1 selected from the group consisting of:

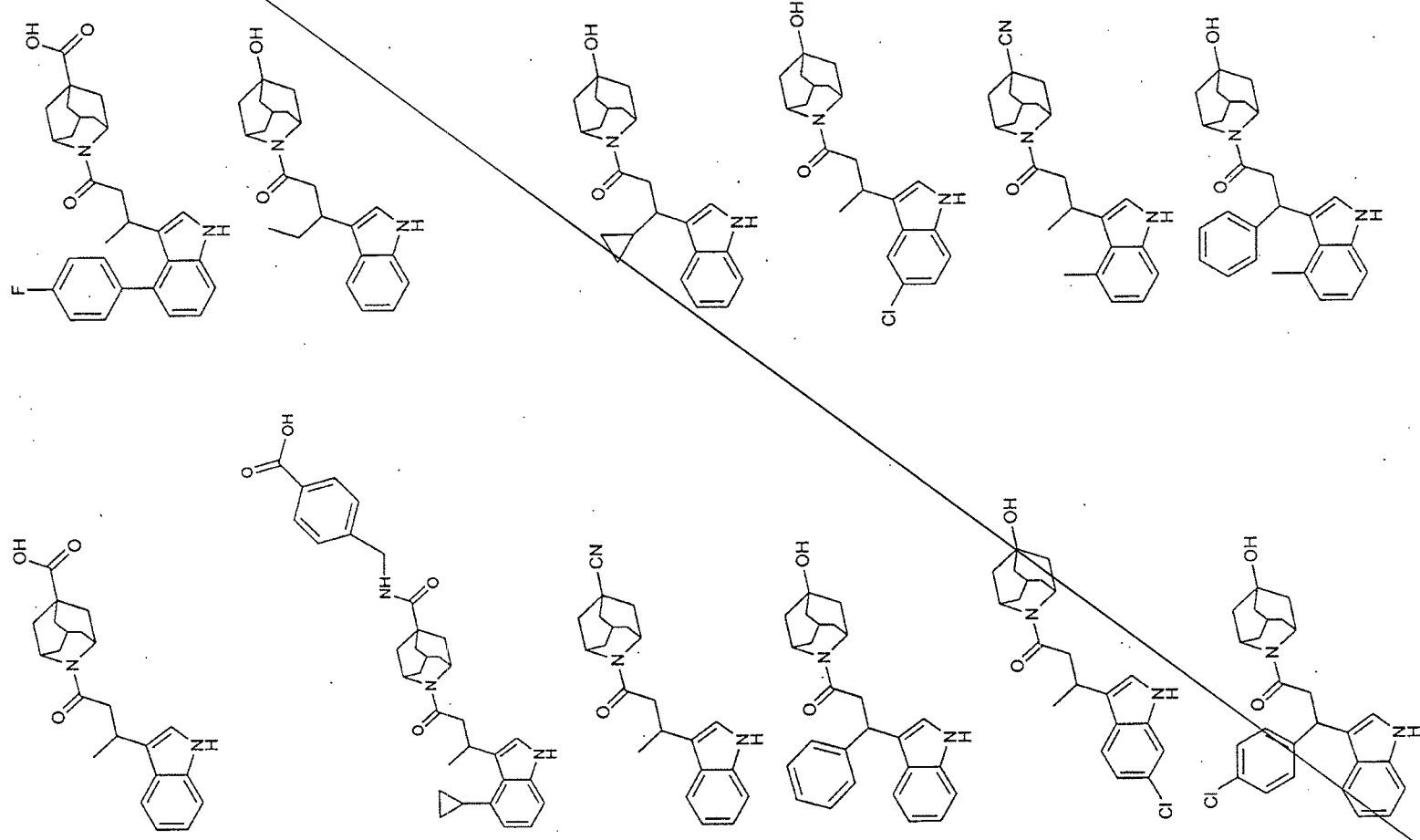


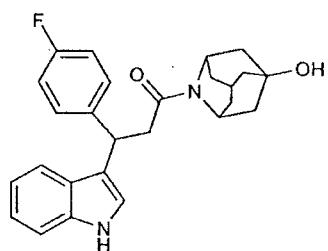
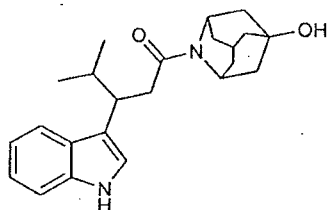
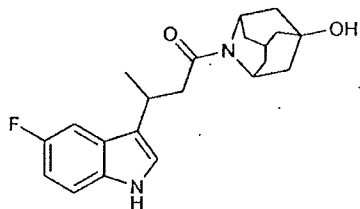
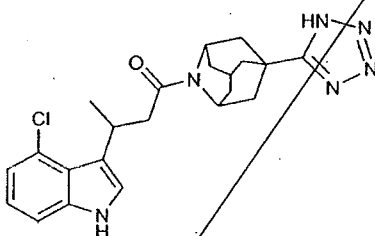
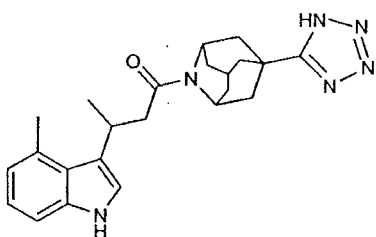
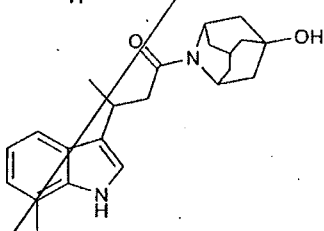
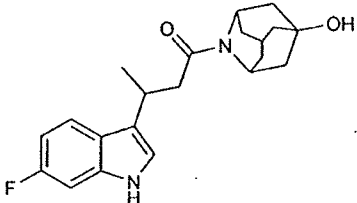
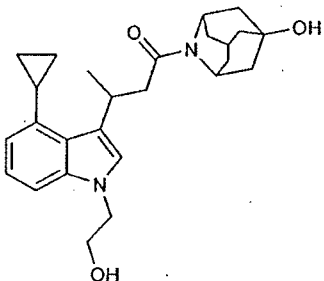
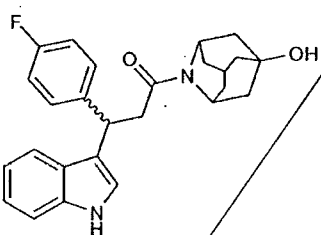
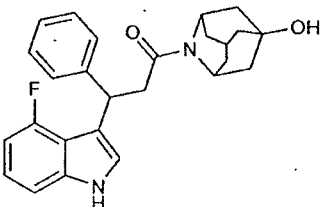
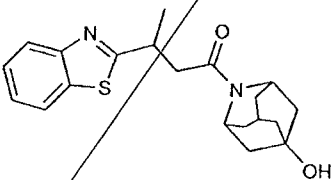
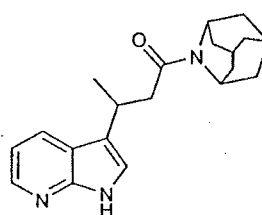


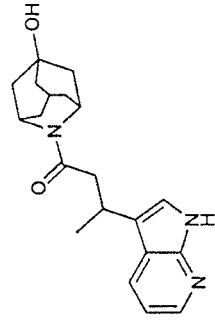
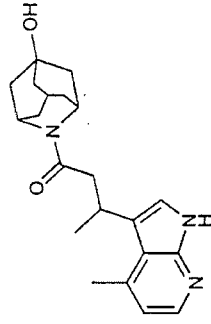
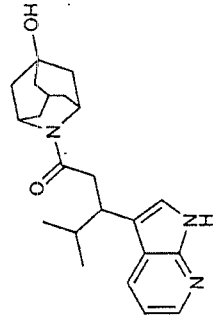
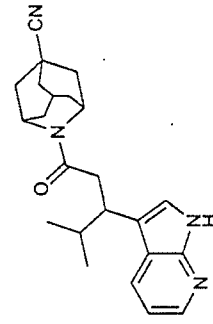
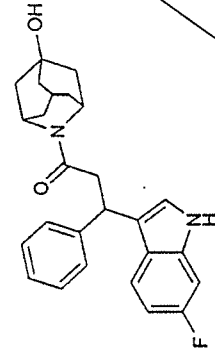
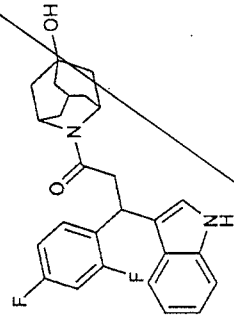
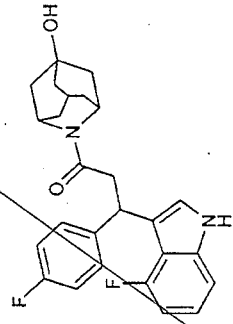
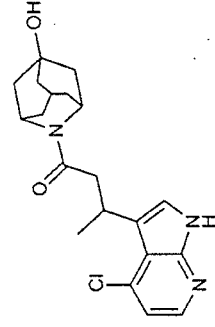
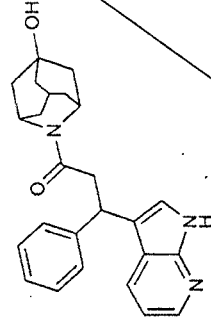
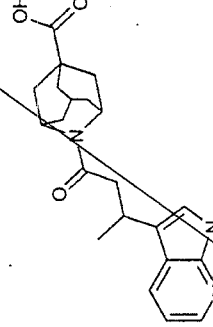
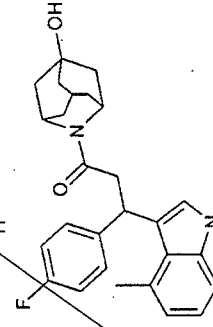
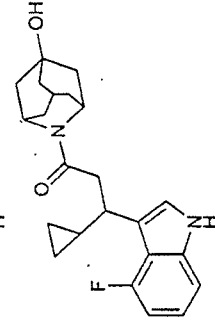
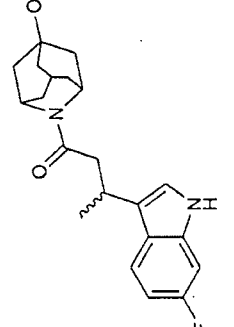
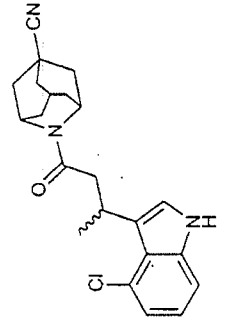


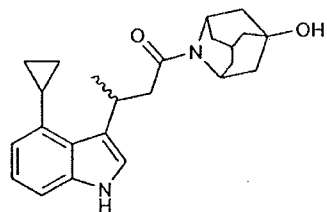
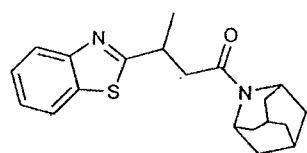
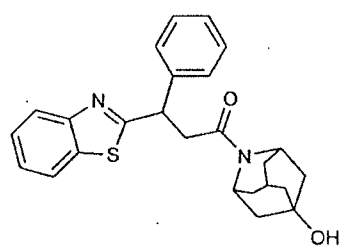
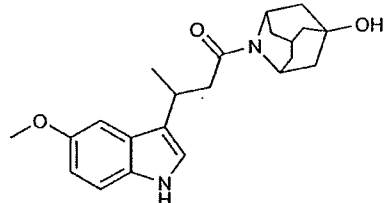
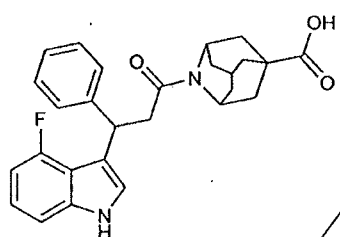
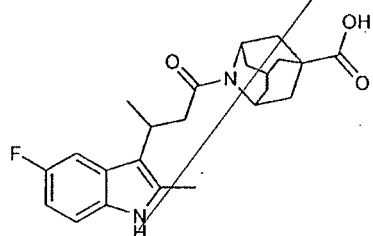
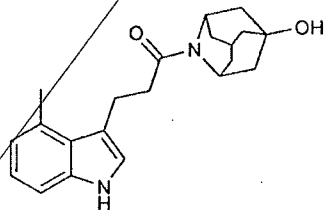
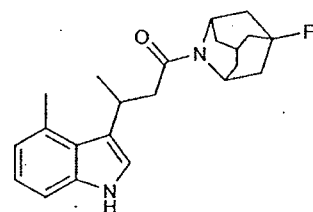
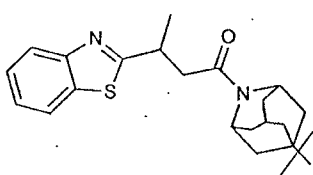
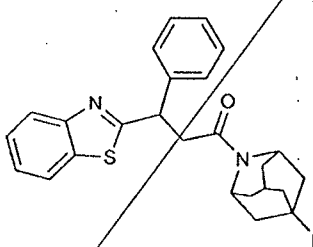
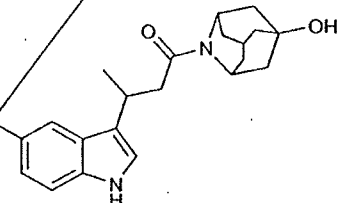
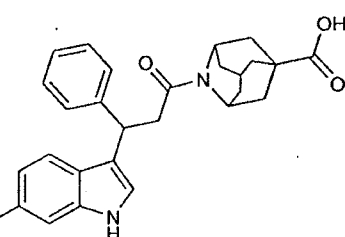
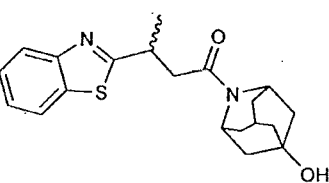
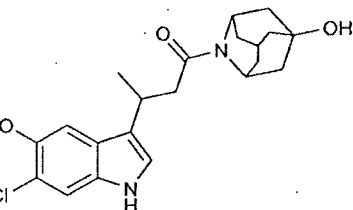


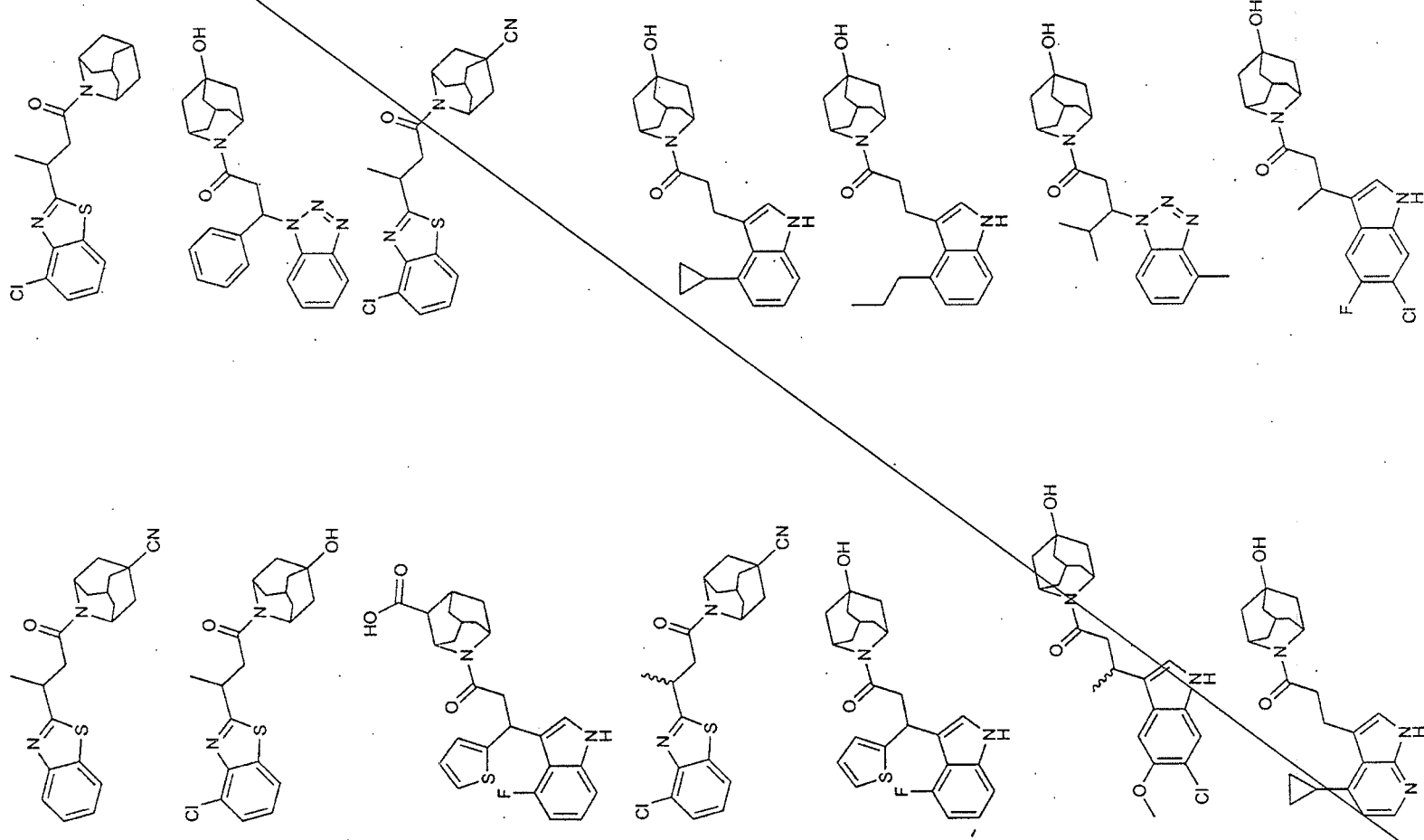


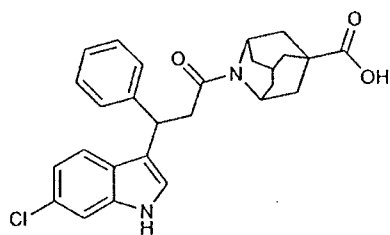
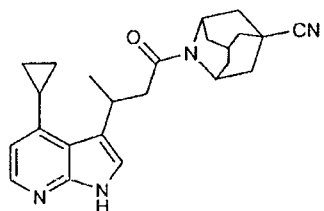
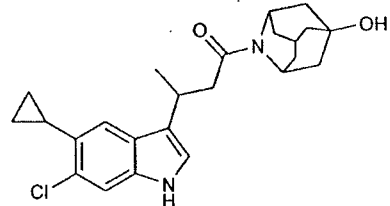
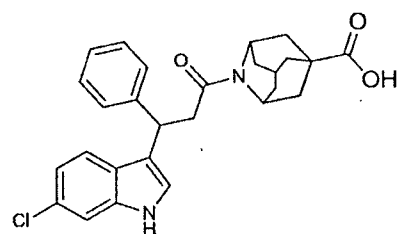
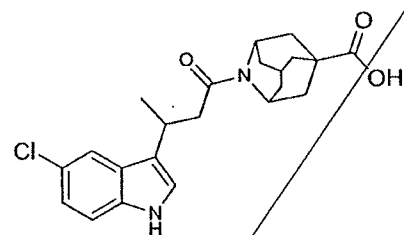
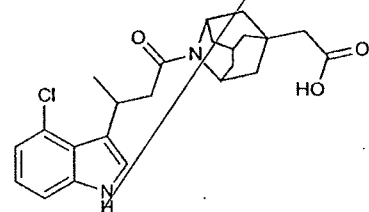
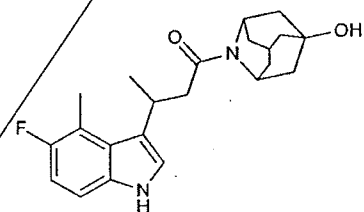
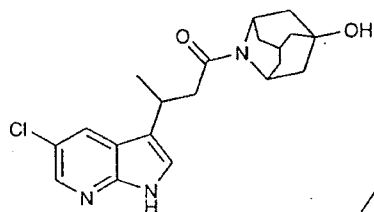
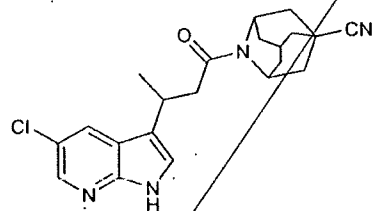
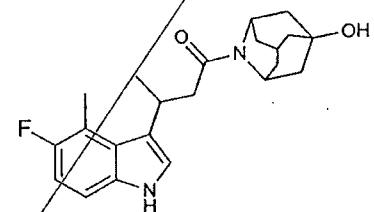
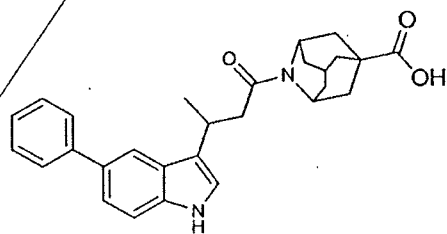
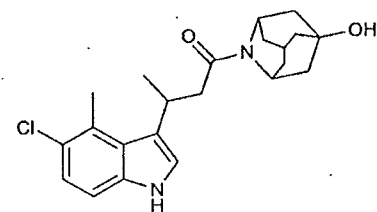
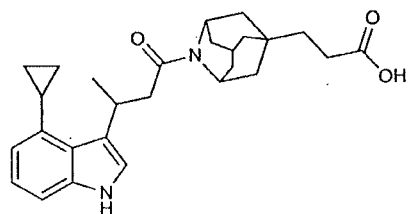
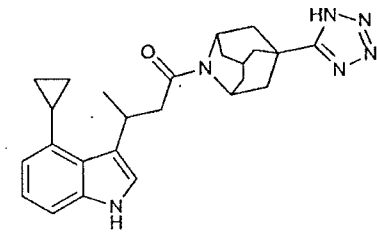


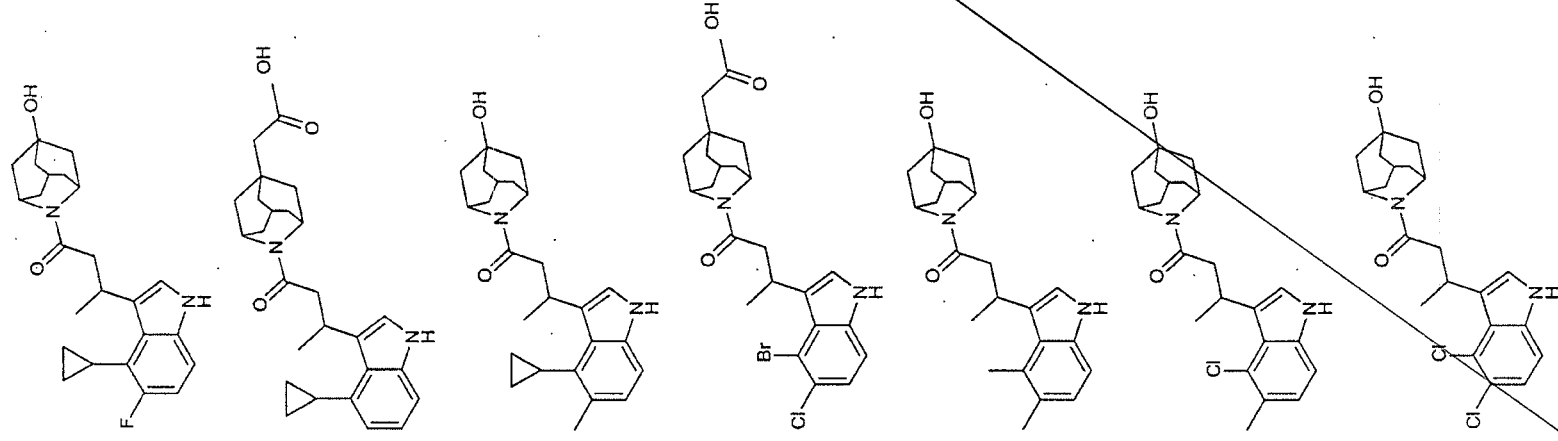
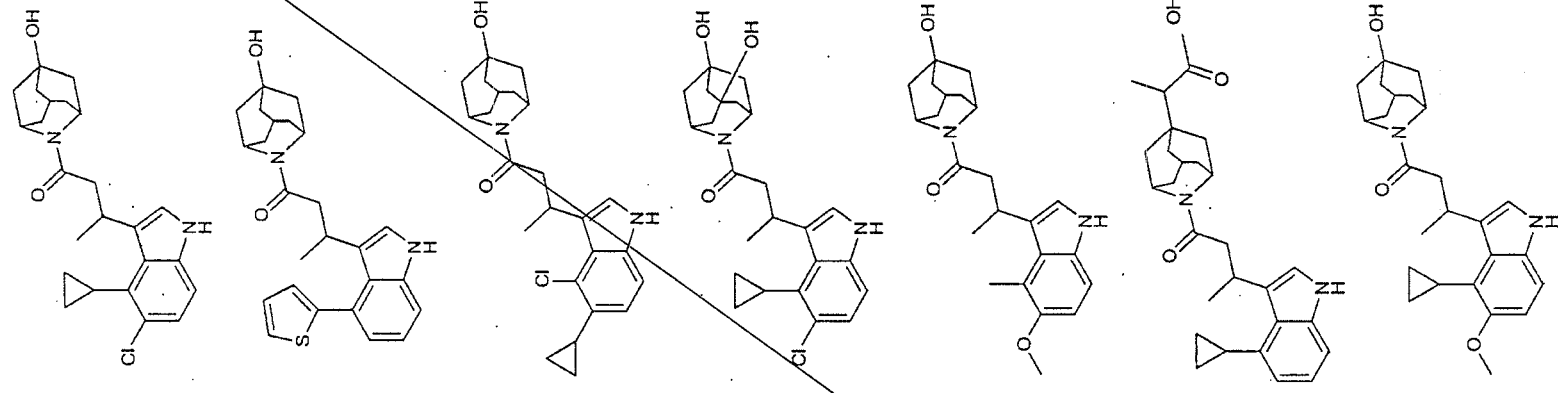


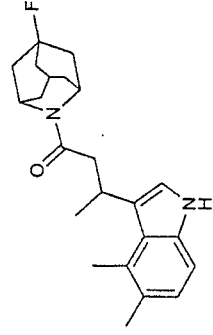
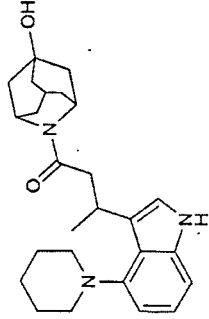
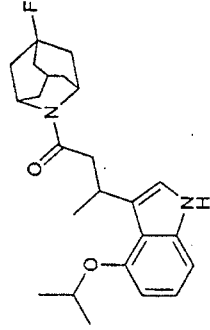
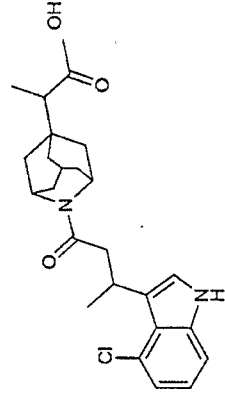
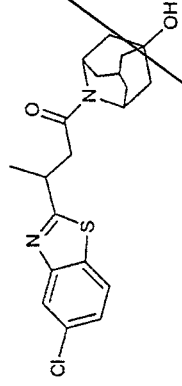
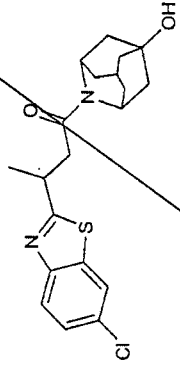
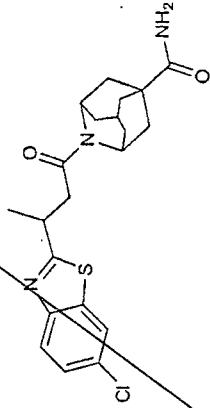
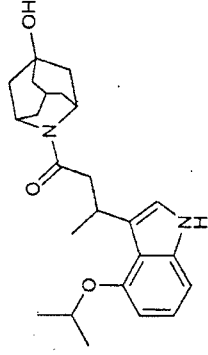
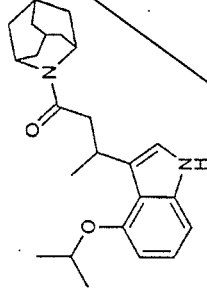
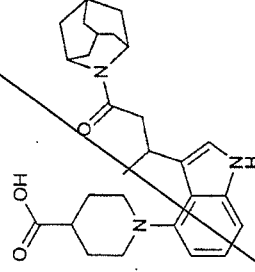
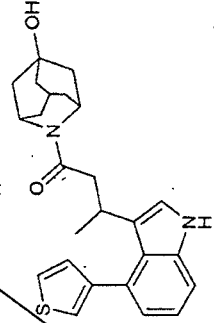
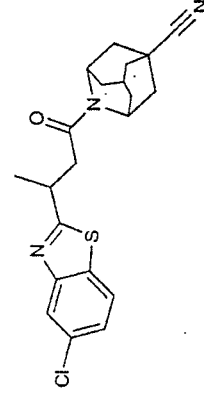
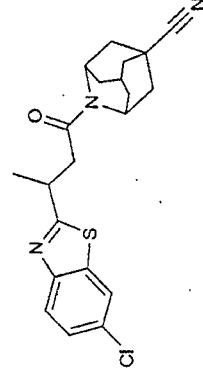
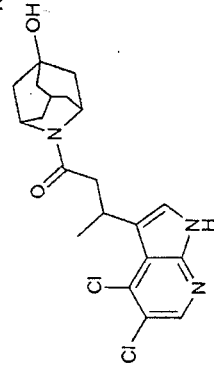


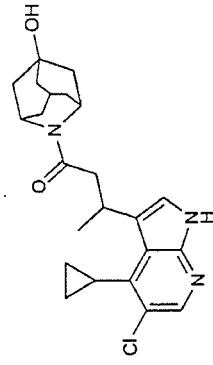
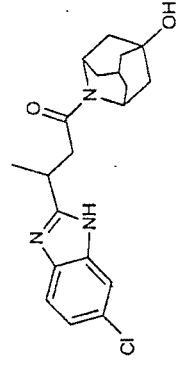
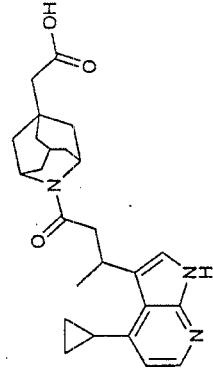
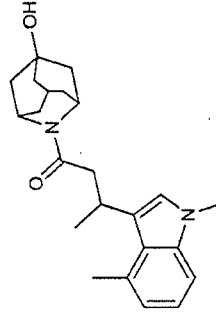
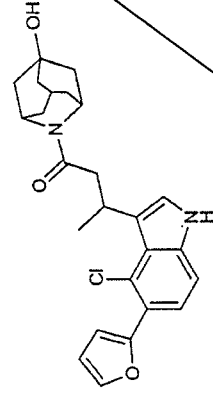
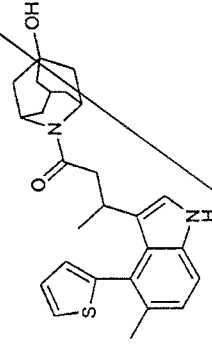
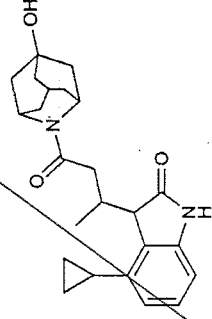
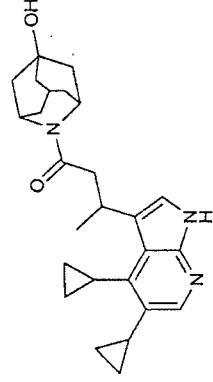
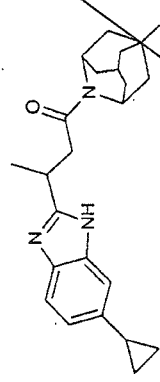
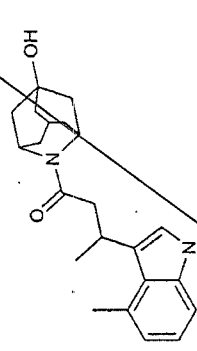
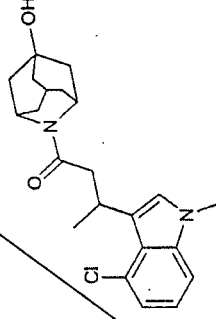
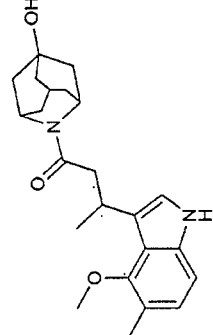
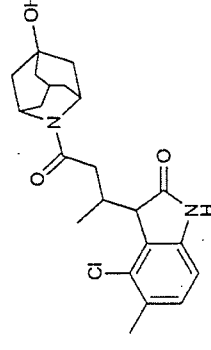
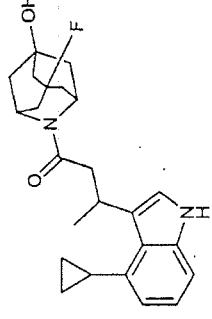


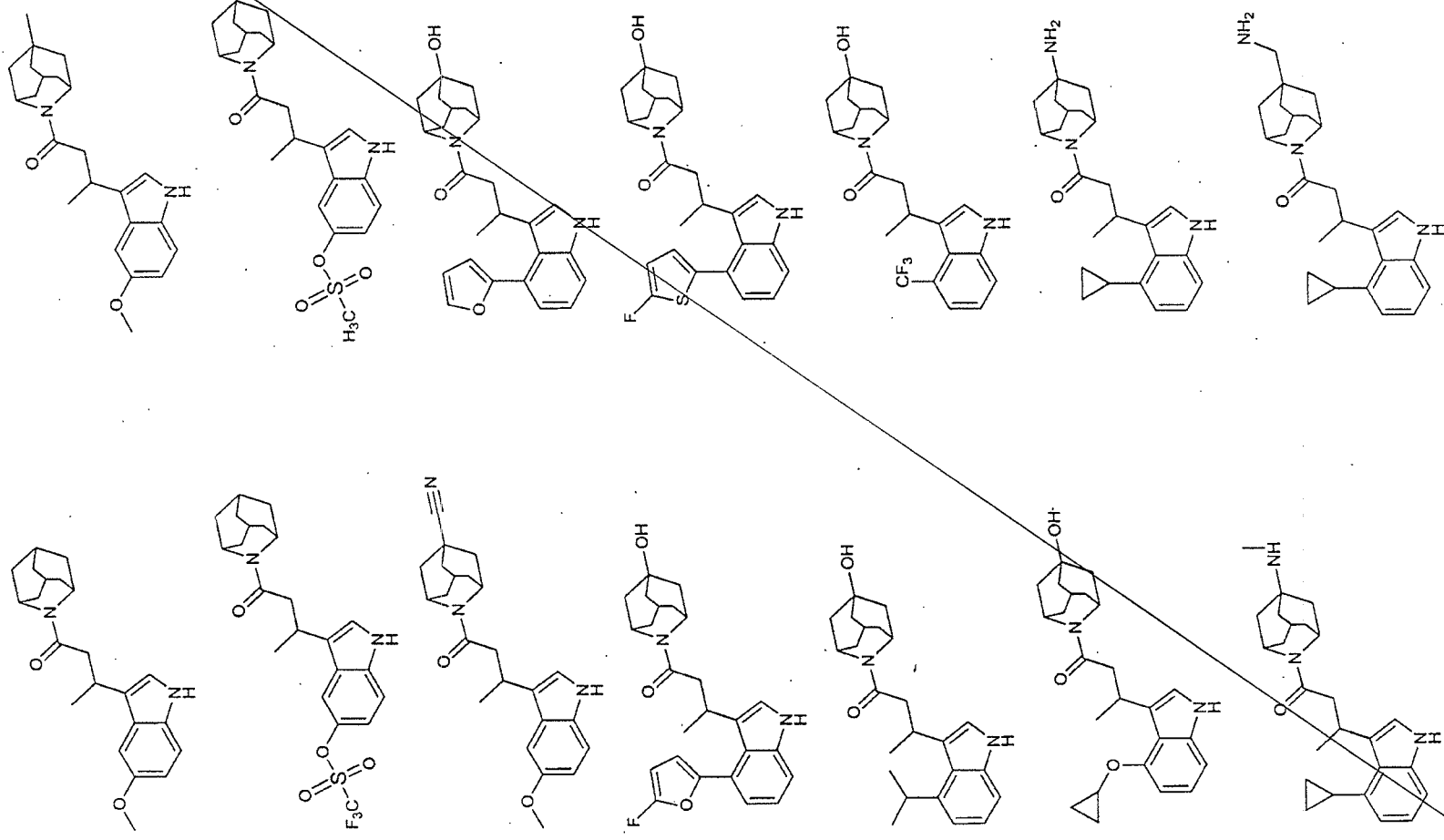


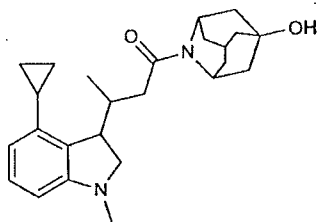
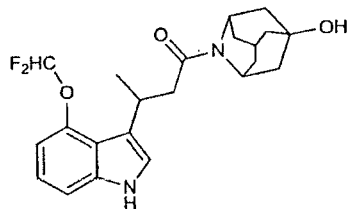
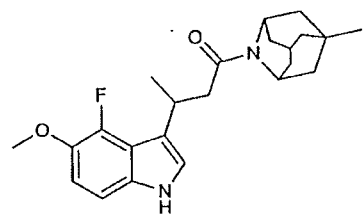
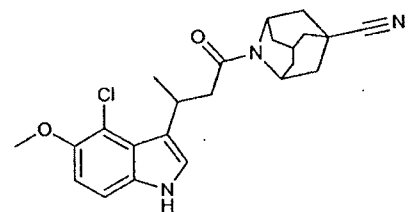
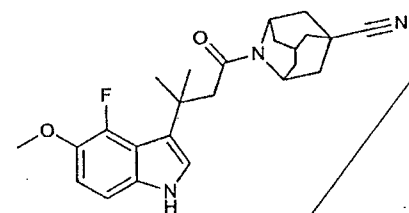
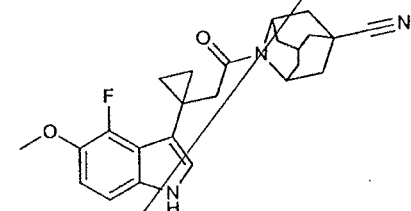
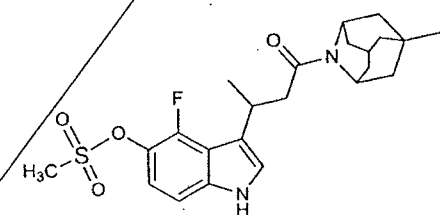
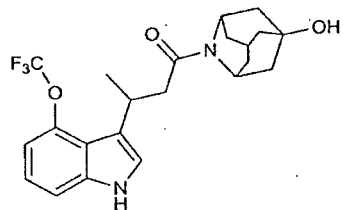
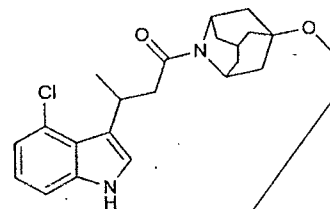
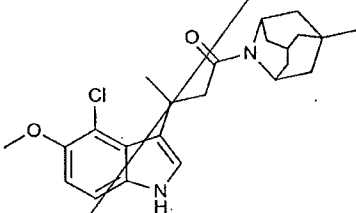
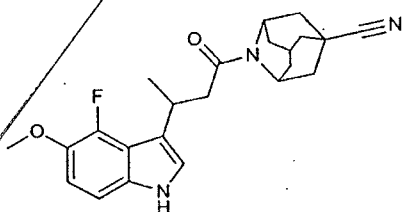
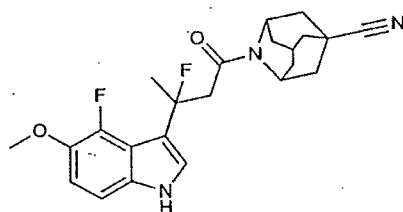
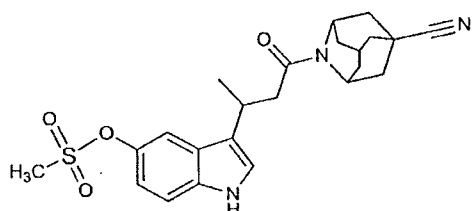
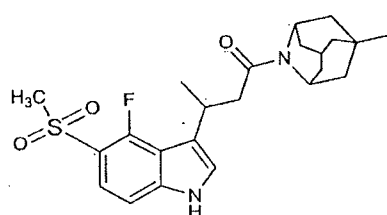


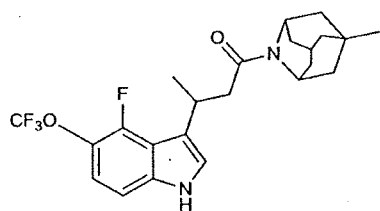
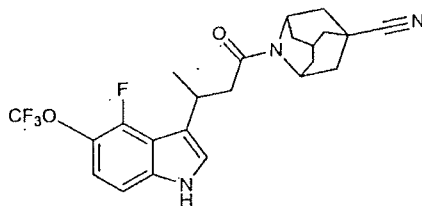
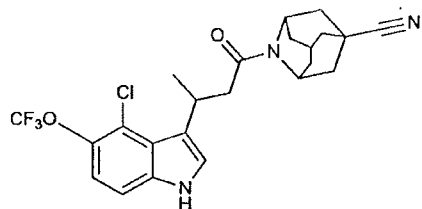
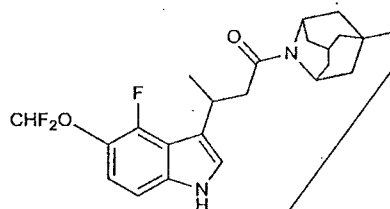
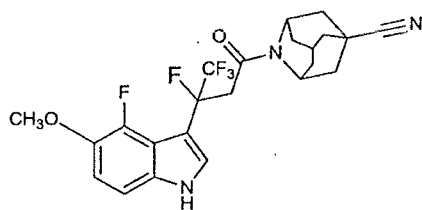
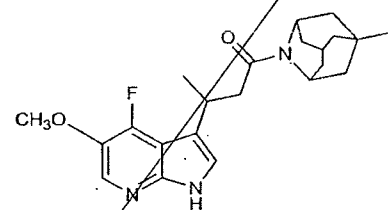
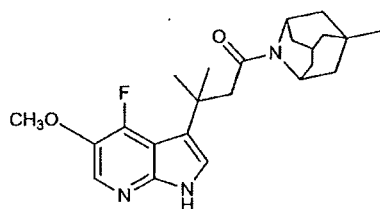
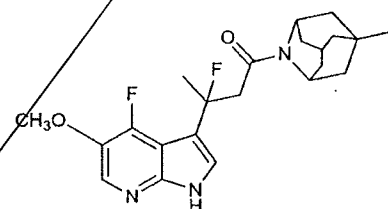
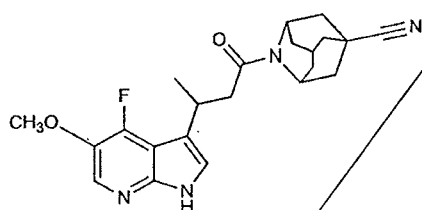
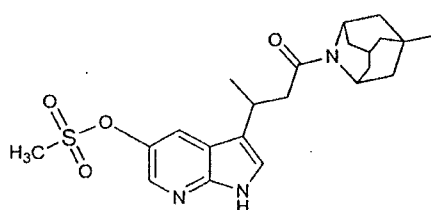
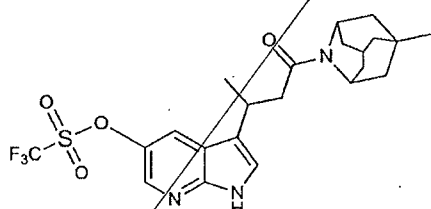
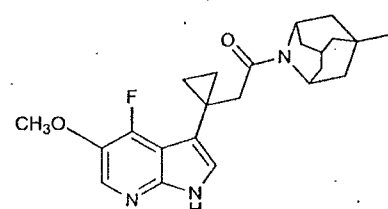
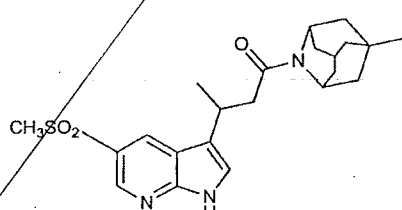
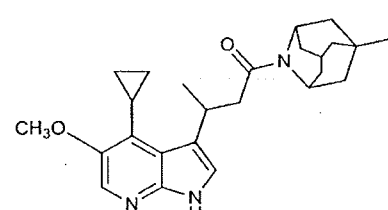


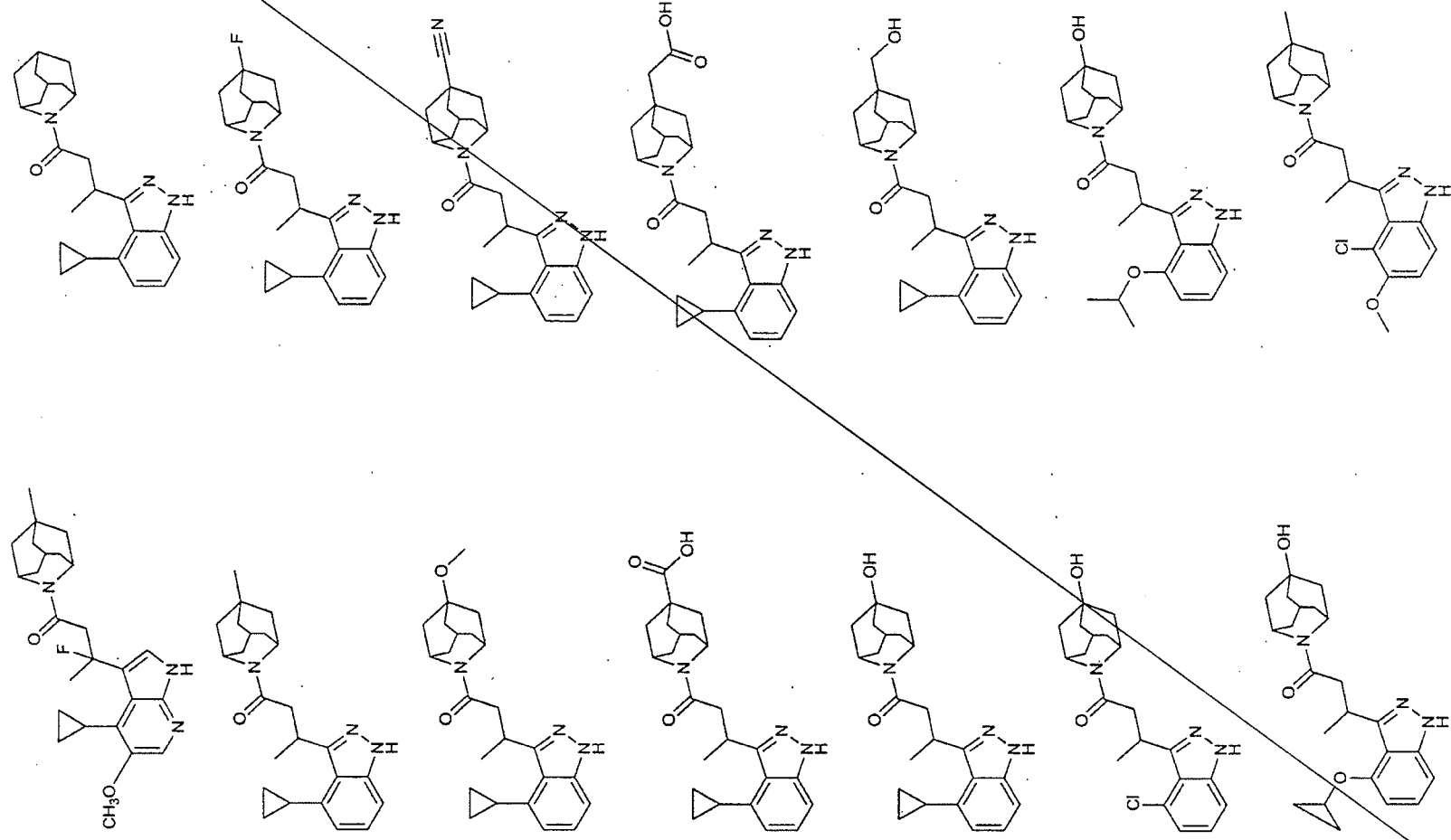


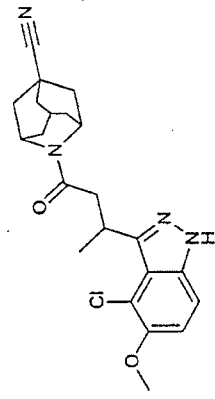
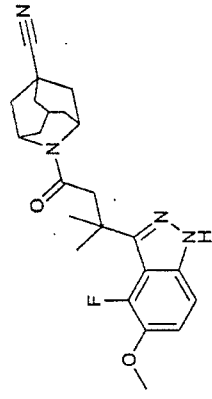
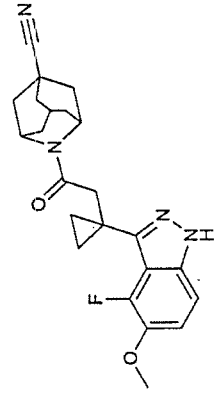
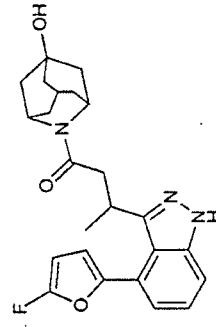
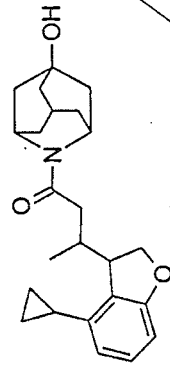
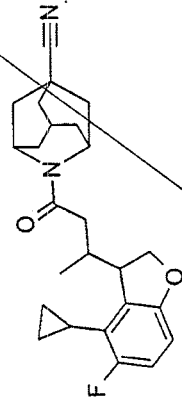
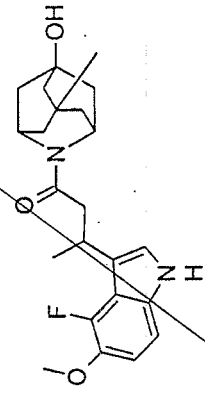
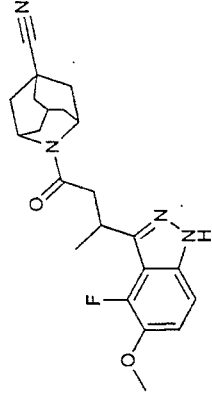
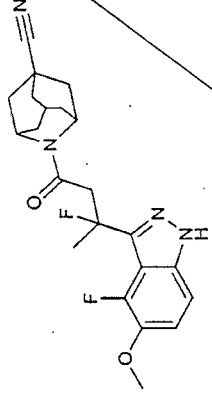
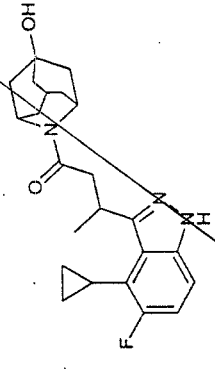
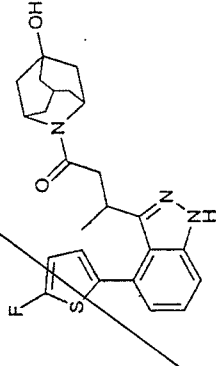
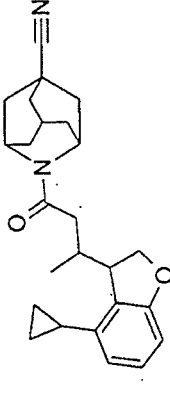
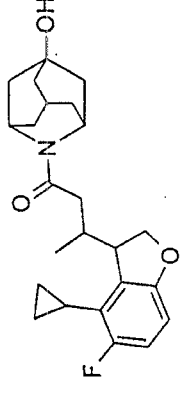
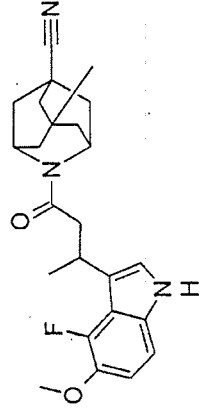


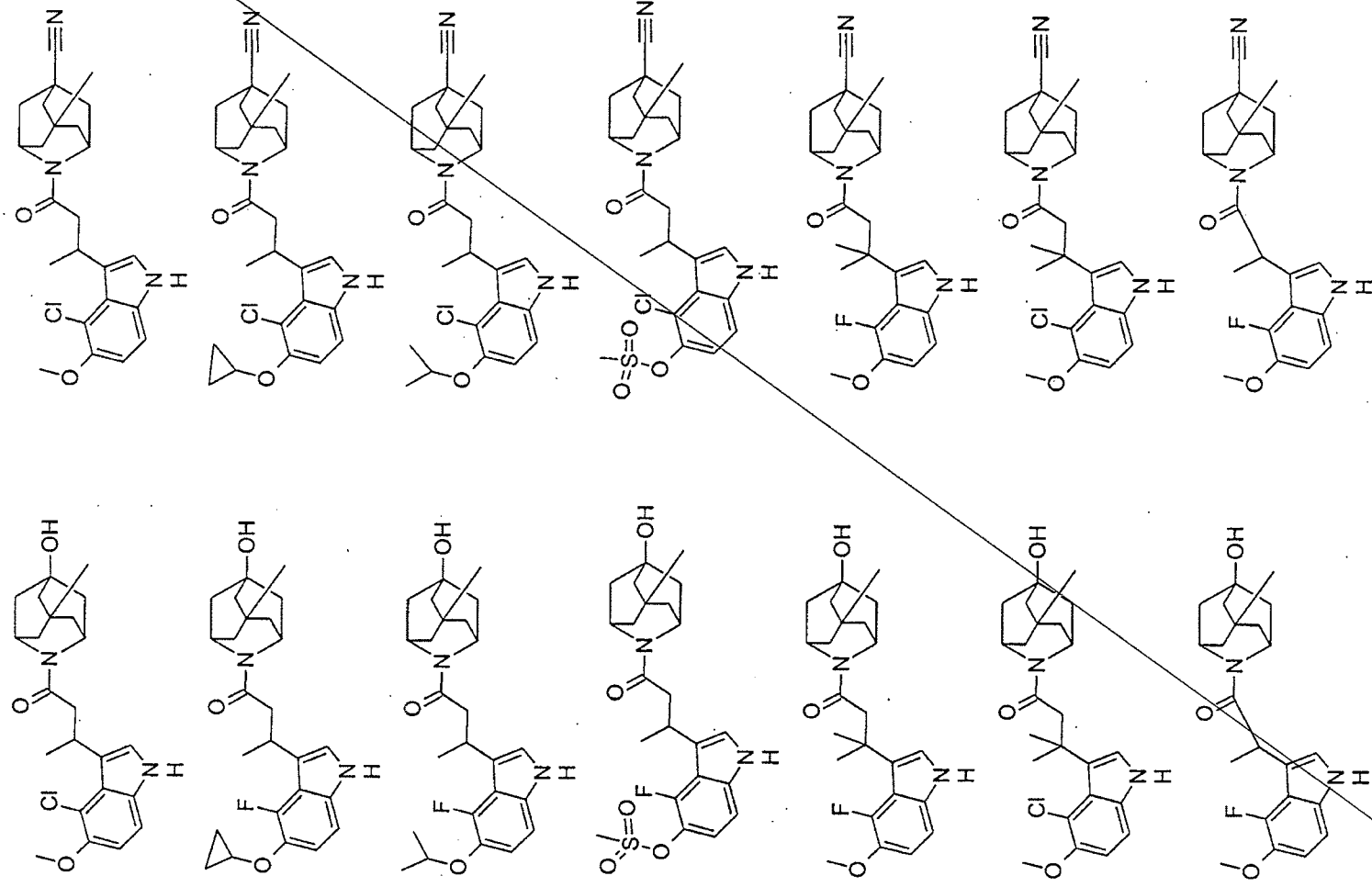


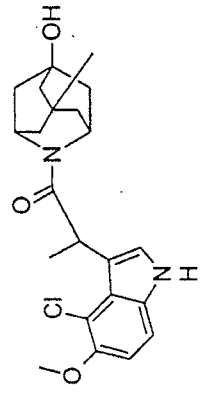
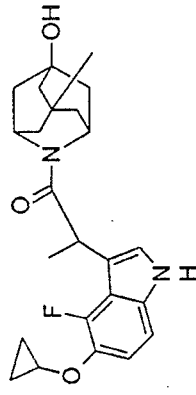
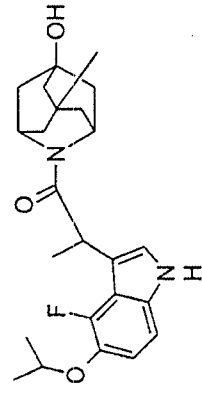
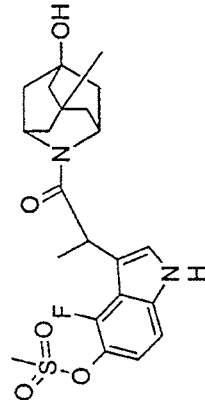
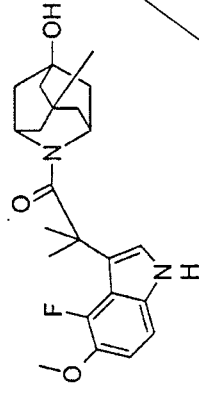
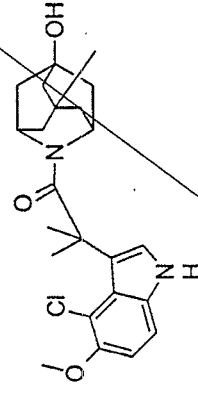
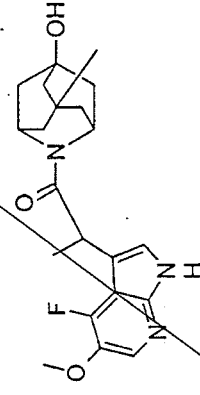
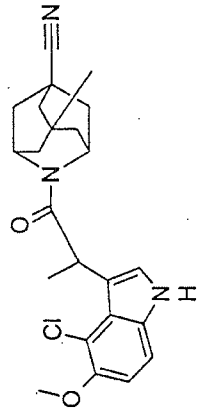
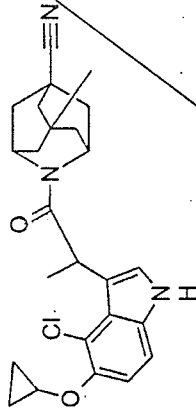
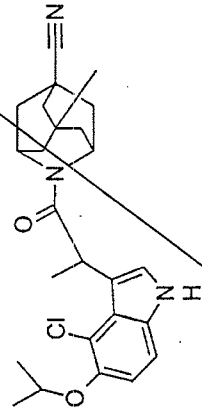
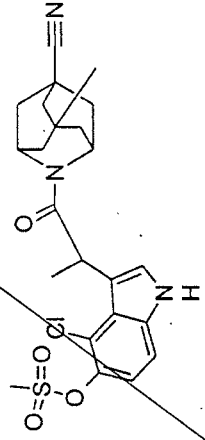
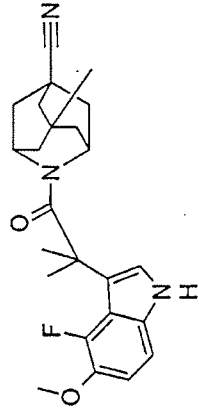
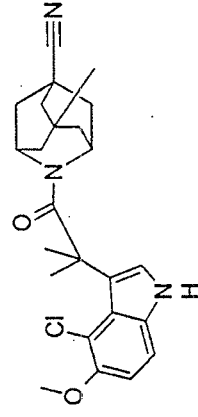
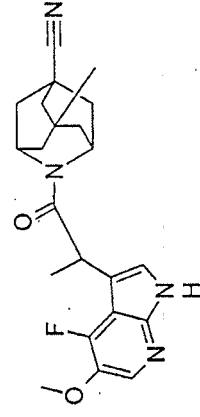


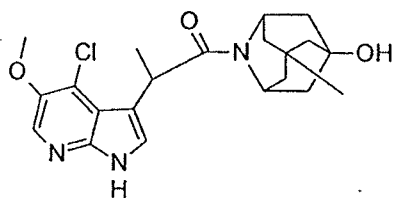
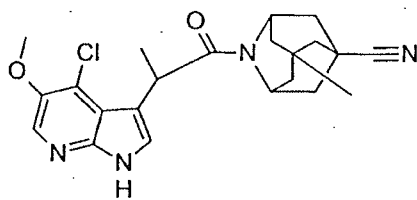
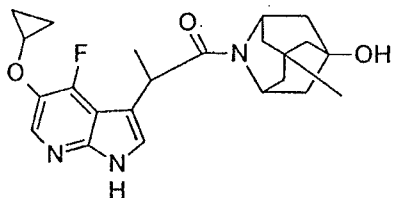
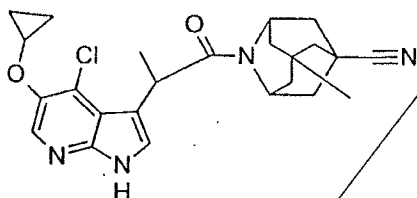
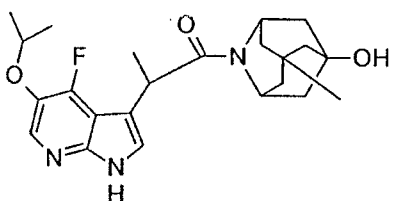
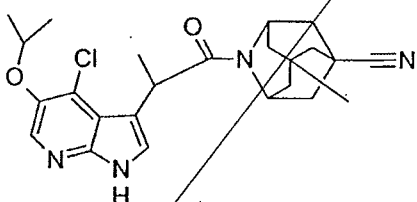
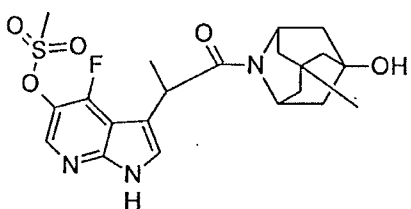
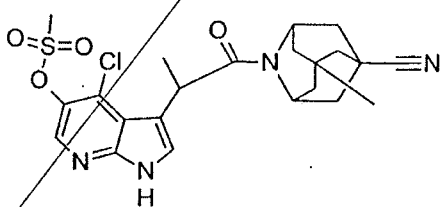
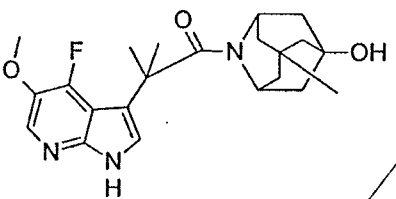
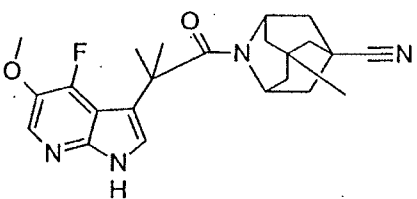
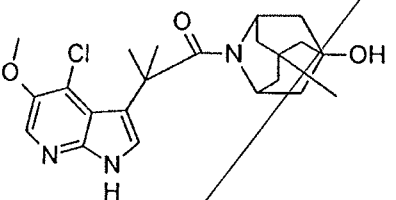
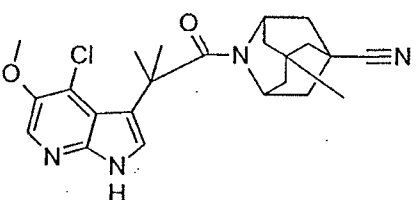
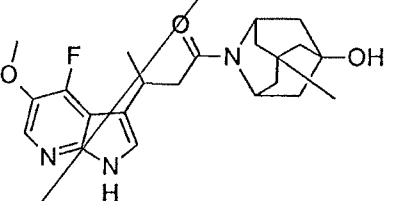
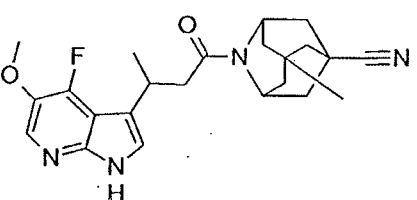


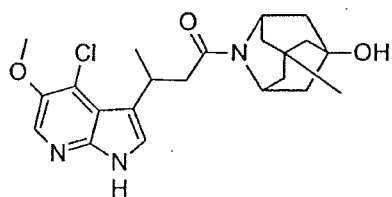
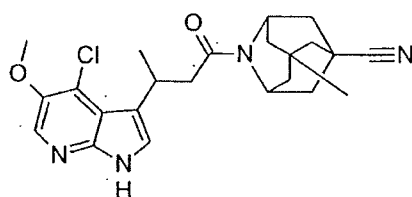
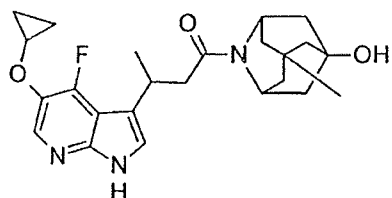
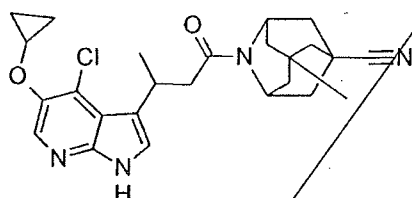
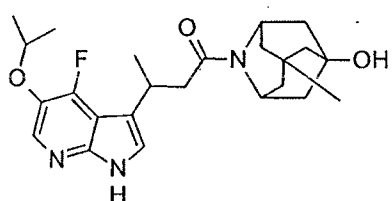
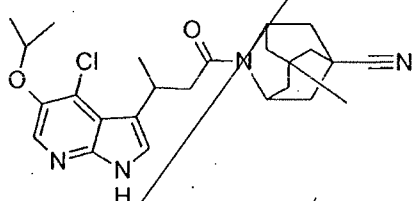
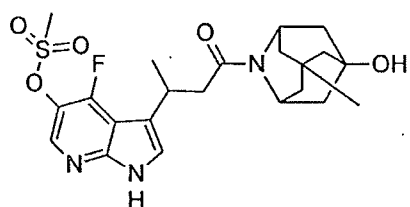
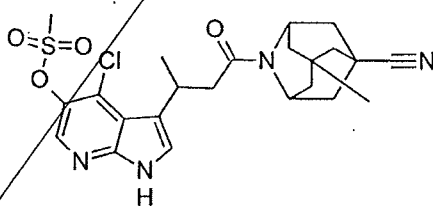
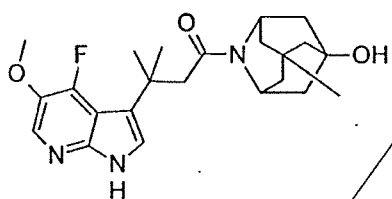
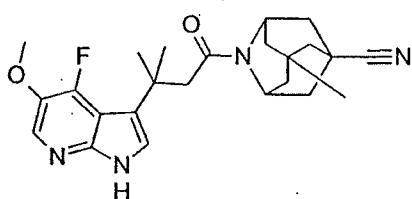
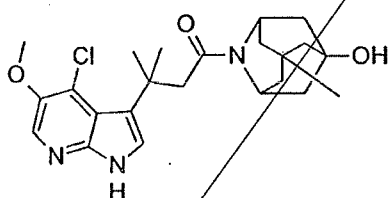
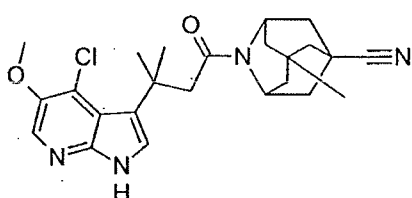
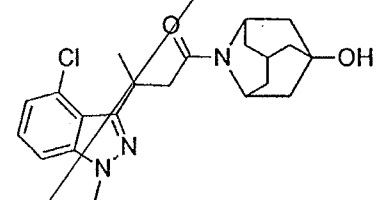
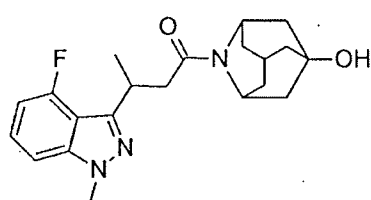


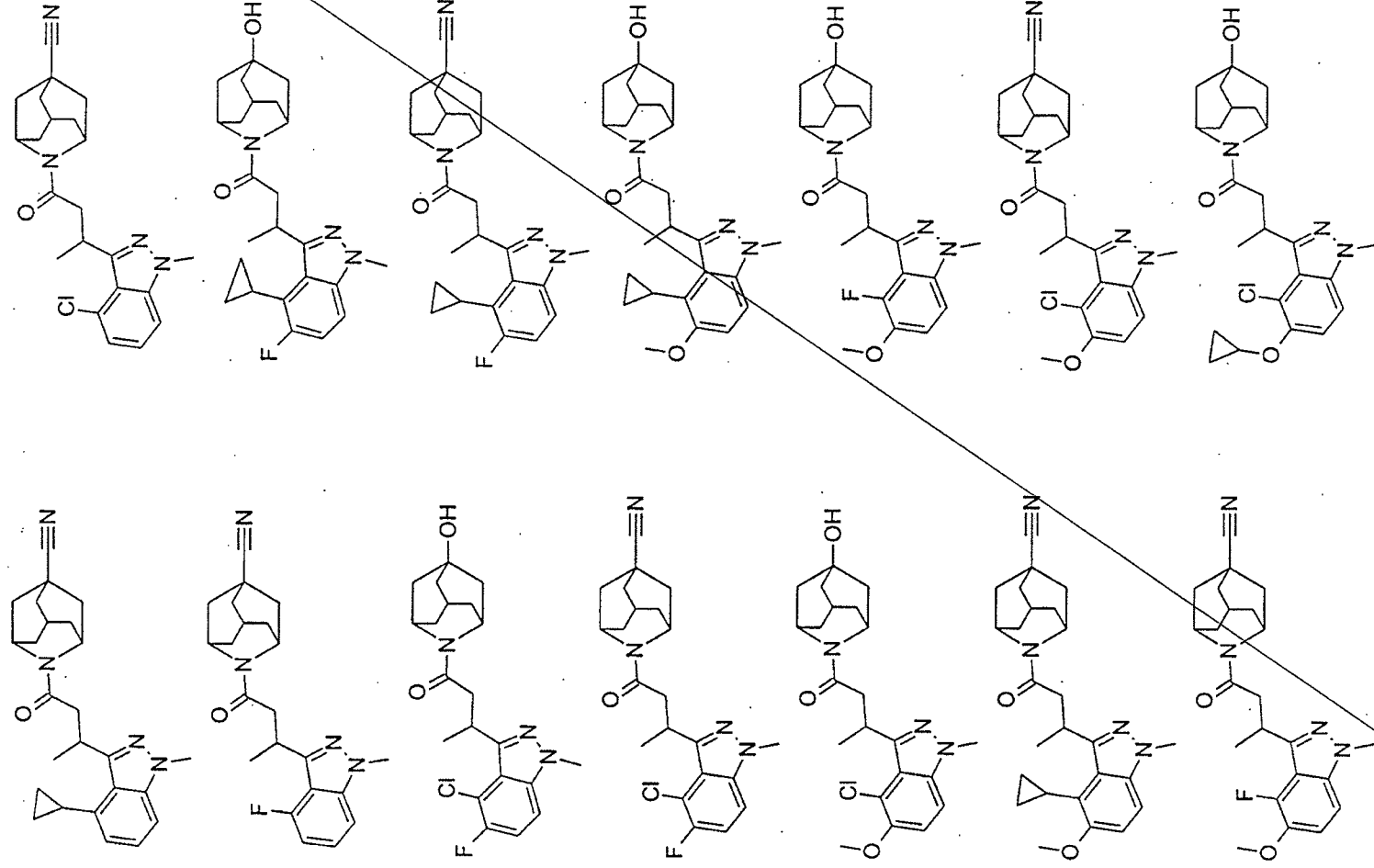


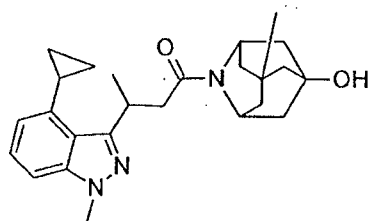
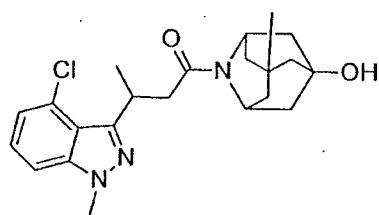
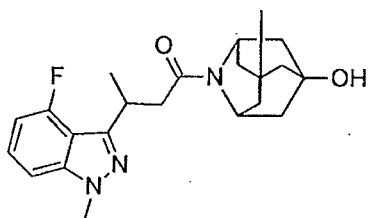
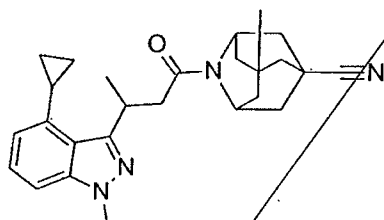
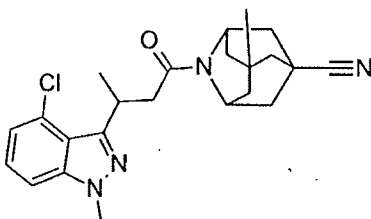
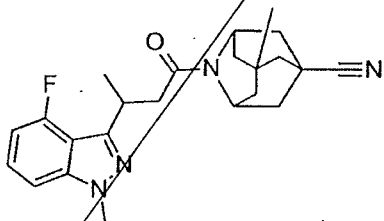
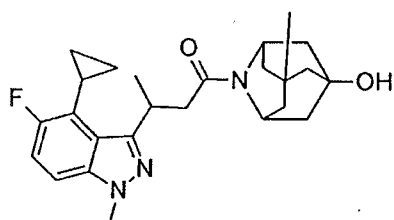
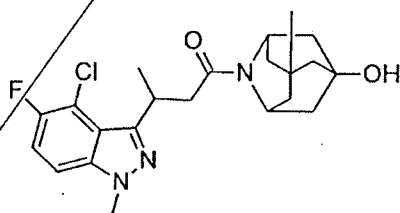
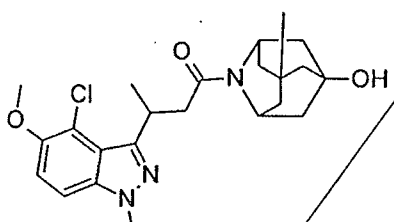
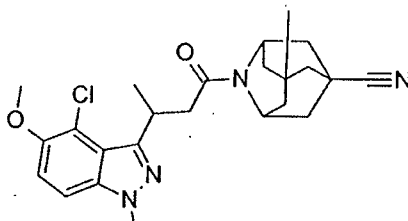
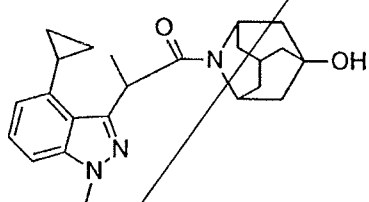
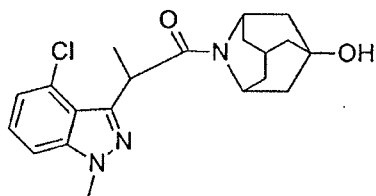
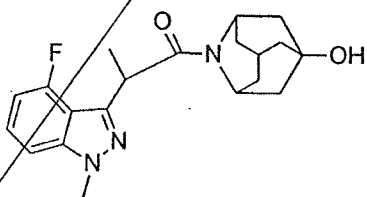
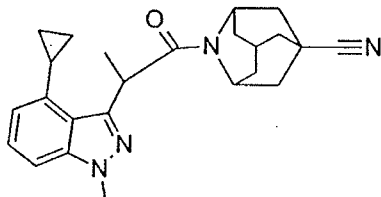


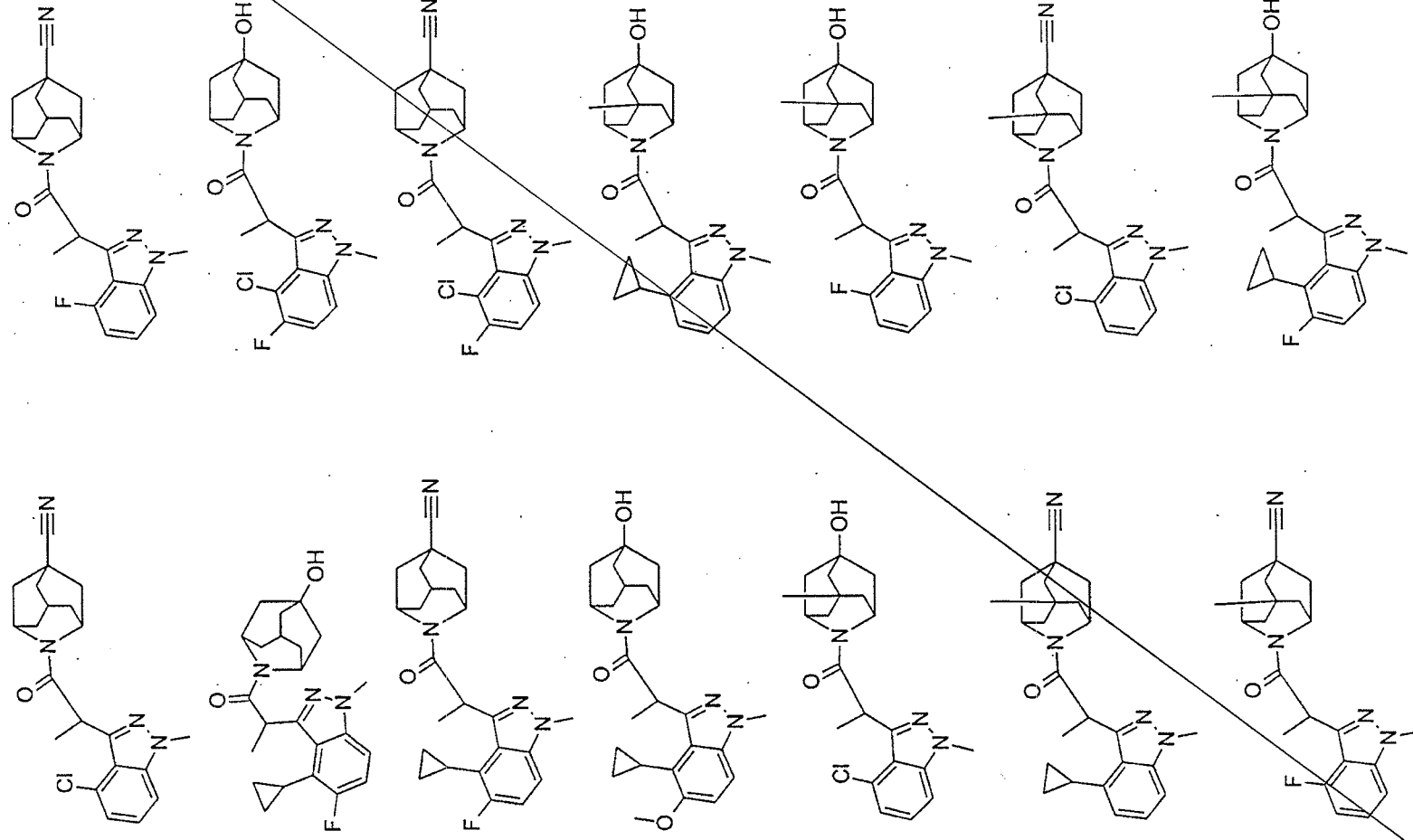


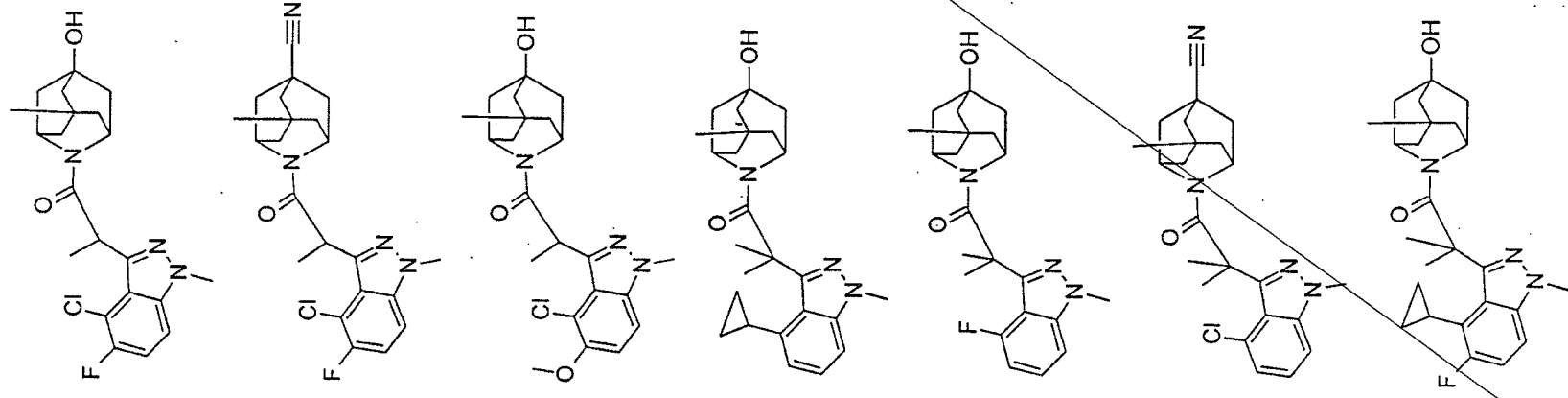
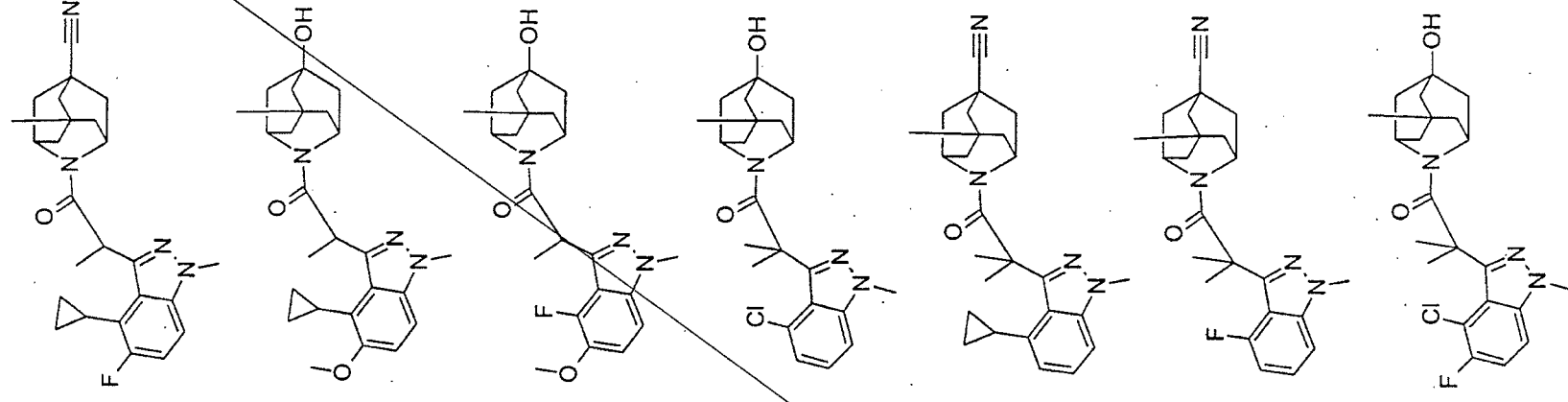


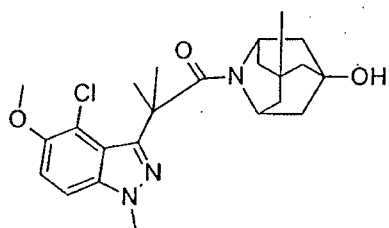
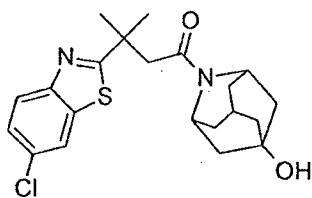
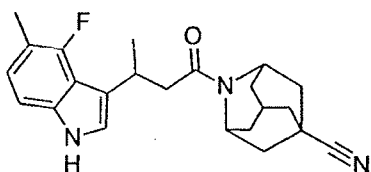
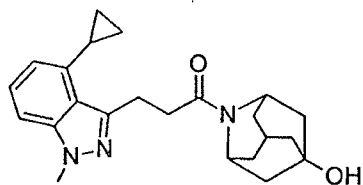
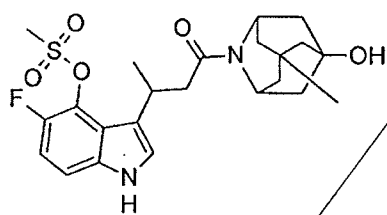
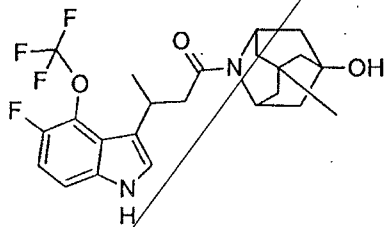
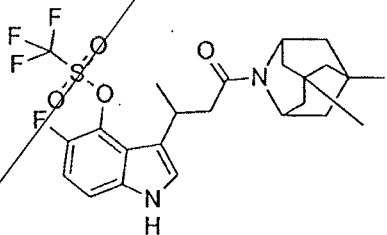
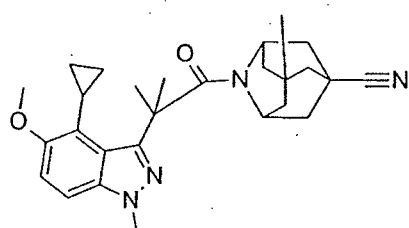
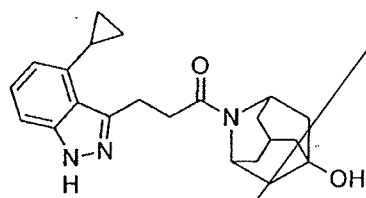
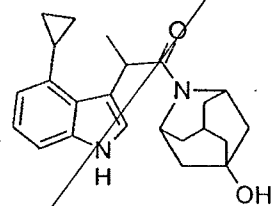
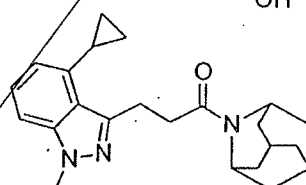
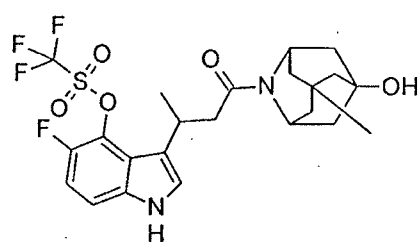
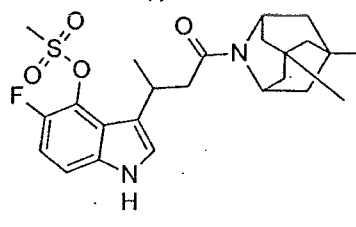
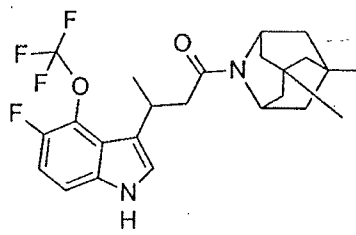


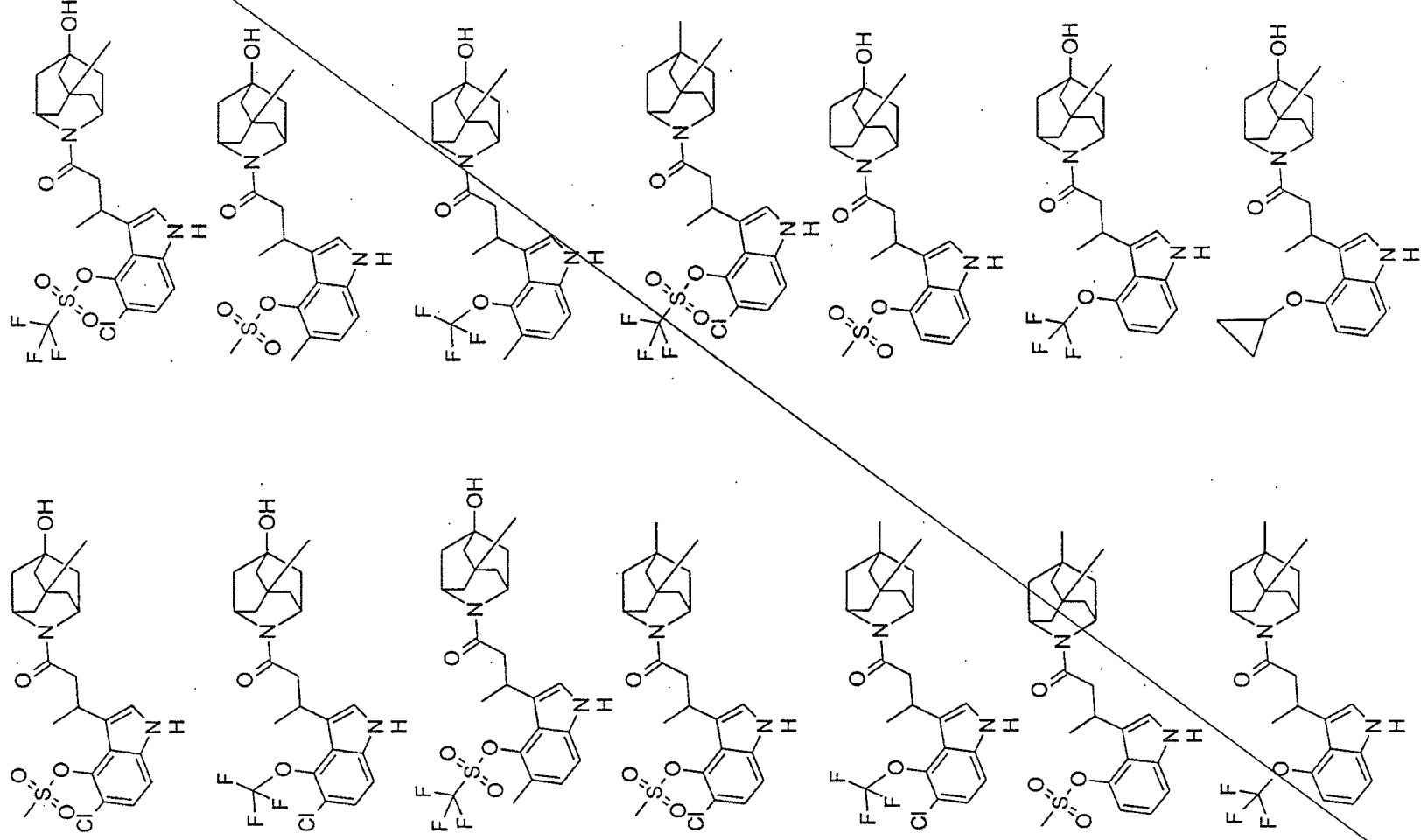


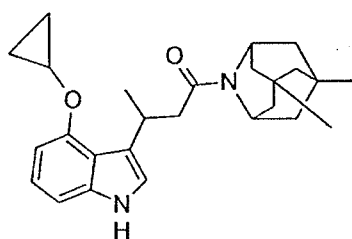
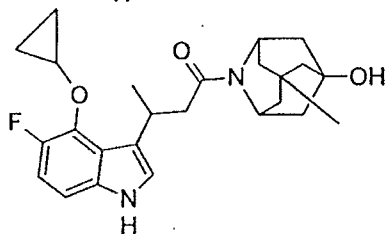
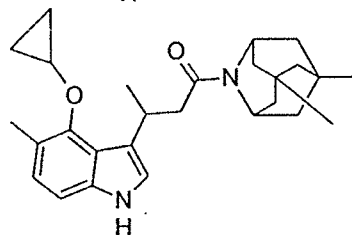
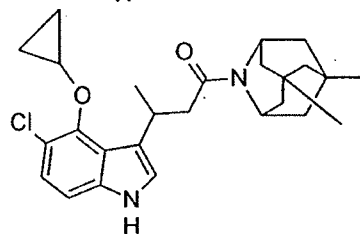
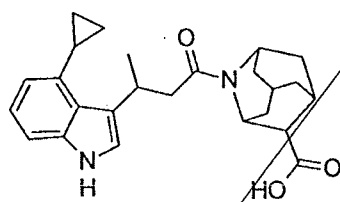
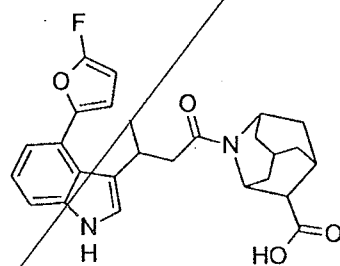
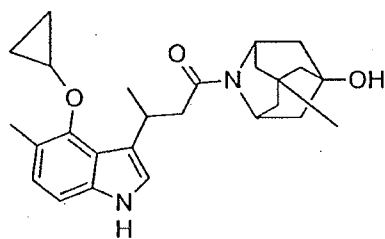
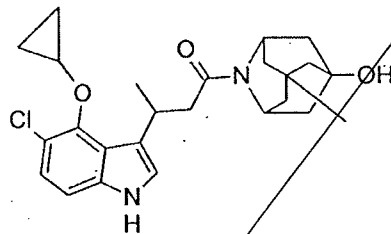
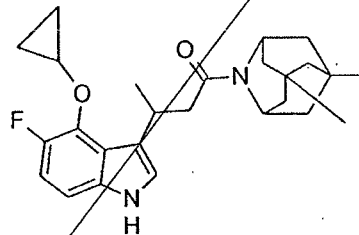
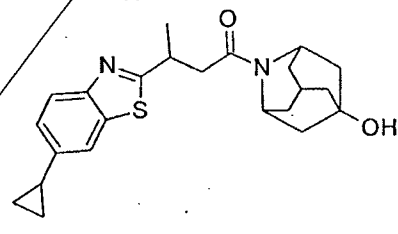
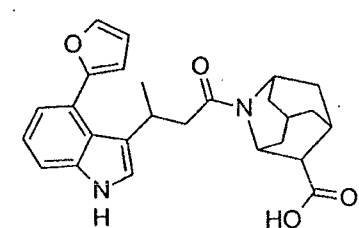
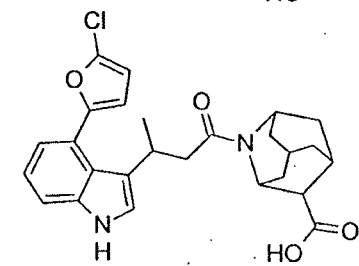


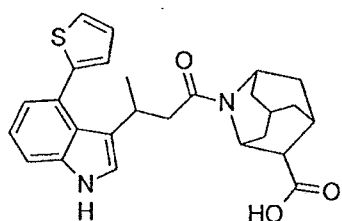
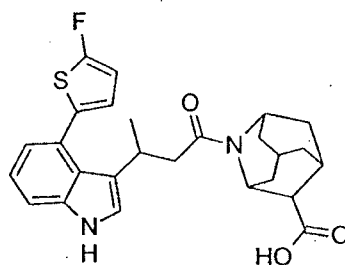
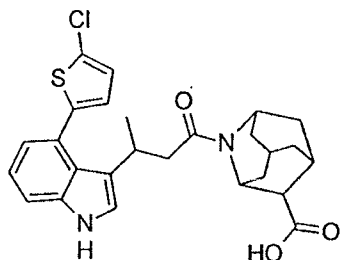
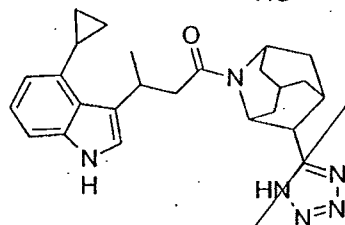
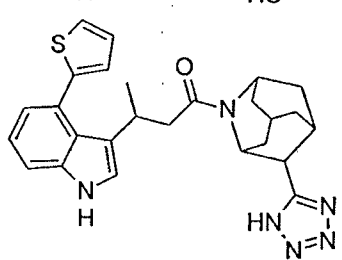
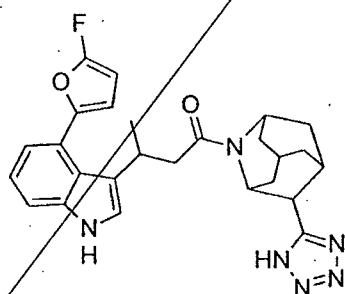
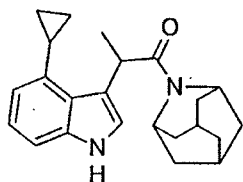












or pharmaceutically acceptable salt, isomer or prodrug thereof.

- 5 17. A pharmaceutical composition including a compound according to any one of claims 1 to 16 and a pharmaceutically acceptable diluent, excipient or carrier.

18. A method of prevention or treatment of a condition in a mammal, the method comprising administering an effective amount of a compound according to any one of claims
10 1 to 16.

19. A method according to claim 18 wherein the condition can be prevented or treated by inhibition of 11 β -HSD1.

- 15 20. A method according to claim 19 wherein the condition is selected from the group consisting of Metabolic syndrome, type 2 diabetes, diabetes as a consequence of obesity,

insulin resistance, hyperglycemia, prandial hyperglycemia, hyperinsulinemia, Inappropriately low insulin secretion, impaired glucose tolerance (IGT), impaired fasting glucose (IFG), increased hepatic glucose production, pediatric diabetes, dyslipidemia, diabetic dyslipidemia, hyperlipidemia, hypertriglyceridemia, hyperlipoproteinemia, hypercholesterolemia, decreased
5 HDL cholesterol, impaired LDL/HDL ratio, other disorders of lipid metabolism, obesity, visceral obesity, hypertension, diabetic late complications, micro-/macroalbuminuria, nephropathy, retinopathy, neuropathy, diabetic ulcers, cardiovascular diseases, arteriosclerosis, atherosclerosis, coronary artery disease, cardiac hypertrophy, myocardial ischemia, heart insufficiency, congestional heart failure, stroke, myocardial infarction,
10 arrhythmia, decreased blood flow, myopathy, loss of muscle tissue, muscle wasting, muscle catabolism and osteoporosis.

21. A method according to claim 19 wherein the condition is selected from the group consisting of metabolic syndrome, diabetes, diabetic late complications, hyperglycemia, low
15 glucose tolerance (IGT), impaired fasting glucose (IFG) hyperinsulinemia, hyperlipidemia, hypertriglyceridemia, hypercholesterolemia, dyslipidemia, obesity, abdominal obesity, glaucoma, hypertension, cardiovascular diseases, arteriosclerosis, atherosclerosis and its sequelae, myopathy, muscle wasting, osteoporosis, glaucoma and dysregulation of intraocular pressure, disorders of lipid metabolism, polycystic ovaries syndrome, retinopathy,
20 nephropathy, neuropathy, osteoporosis, osteoarthritis, dementia, depression, neurodegenerative disease, psychiatric disorders, Cushing's Disease, Cushing's syndrome, viral diseases, and inflammatory diseases.

22. A method according to claim 21 wherein the condition is diabetes.

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23. A method according to claim 21 wherein the condition is type II diabetes.

24. The method of claim 24, wherein the compound is administered in combination with an adjuvant.

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25. The method of claim 24, wherein the adjuvant is selected from the group consisting of dipeptidyl peptidase-IV (DP-IV) inhibitors; (b) insulin sensitizing agents; (c) insulin and insulin mimetics; (d) sulfonylureas and other insulin secretagogues; (e) alpha-glucosidase inhibitors; (f) GLP-1, GLP-1 analogs, and GLP-1 receptor agonists; and combinations thereof.

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26. The method of claim 25, wherein the insulin sensitizing agents are selected from the group consisting of (i) PPAR-gamma-agonists, (ii) PPAR-alpha-agonists, (iii) PPAR-alpha/gamma-dual agonists, (iv) biguanides, and combinations thereof.
- 5 27. Use of a compound according to claim 1 in the preparation of a medicament.
28. A use according to claim 27 wherein the medicament is for treatment of a condition that can be prevented or treated by inhibition of 11 β -HSD1.
- 10 29. A use according to claim 28 wherein the condition is selected from the group consisting of Metabolic syndrome, type 2 diabetes, diabetes as a consequence of obesity, insulin resistance, hyperglycemia, prandial hyperglycemia, hyperinsulinemia, Inappropriately low insulin secretion, impaired glucose tolerance (IGT), impaired fasting glucose (IFG), increased hepatic glucose production, pediatric diabetes, dyslipidemia, diabetic dyslipidemia, hyperlipidemia, hypertriglyceridemia, hyperlipoproteinemia, hypercholesterolemia, decreased HDL cholesterol, impaired LDL/HDL ratio, other disorders of lipid metabolism, obesity, visceral obesity, hypertension, diabetic late complications, micro-/macroalbuminuria, nephropathy, retinopathy, neuropathy, diabetic ulcers, cardiovascular diseases, arteriosclerosis, atherosclerosis, coronary artery disease, cardiac hypertrophy, myocardial ischemia, heart insufficiency, congestional heart failure, stroke, myocardial infarction, arrhythmia, decreased blood flow, myopathy, loss of muscle tissue, muscle wasting, muscle catabolism and osteoporosis.
- 15 30. A use according to claim 28 wherein the condition is selected from the group consisting of metabolic syndrome, diabetes, diabetic late complications, hyperglycemia, low glucose tolerance (IGT), impaired fasting glucose (IFG) hyperinsulinemia, hyperlipidemia, hypertriglyceridemia, hypercholesterolemia, dyslipidemia, obesity, abdominal obesity, glaucoma, hypertension, cardiovascular diseases, arteriosclerosis, atherosclerosis and its sequelae, myopathy, muscle wasting, osteoporosis, glaucoma and dysregulation of intraocular pressure, disorders of lipid metabolism, polycystic ovaries syndrome, retinopathy, nephropathy, neuropathy, osteoporosis, osteoarthritis, dementia, depression, neurodegenerative disease, psychiatric disorders, Cushing's Disease, Cushing's syndrome, viral diseases, and inflammatory diseases.
- 30 31. A use according to claim 28 wherein the condition is diabetes.
- 35 32. A use according to claim 28 wherein the condition is type II diabetes.

33. A use according to claim 27 or 28, wherein the medicament contains an adjuvant.
34. A use according to claim 33, wherein the adjuvant is selected from the group consisting of dipeptidyl peptidase-IV (DP-IV) inhibitors; (b) insulin sensitizing agents; (c) insulin and insulin mimetics; (d) sulfonylureas and other insulin secretagogues; (e) alpha-glucosidase inhibitors; (f) GLP-1, GLP-1 analogs, and GLP-1 receptor agonists; and combinations thereof.
35. A use according to claim 34 wherein the insulin sensitizing agents are selected from the group consisting of (i) PPAR-gamma-agonists, (ii) PPAR-alpha-agonists, (iii) PPAR-alpha/gamma-dual agonists, (iv) biguanides, and combinations thereof.
36. A compound according to claim 1 substantially as hereinbefore described with reference to any of the examples.